PROGRESSIVE

MEDICINE
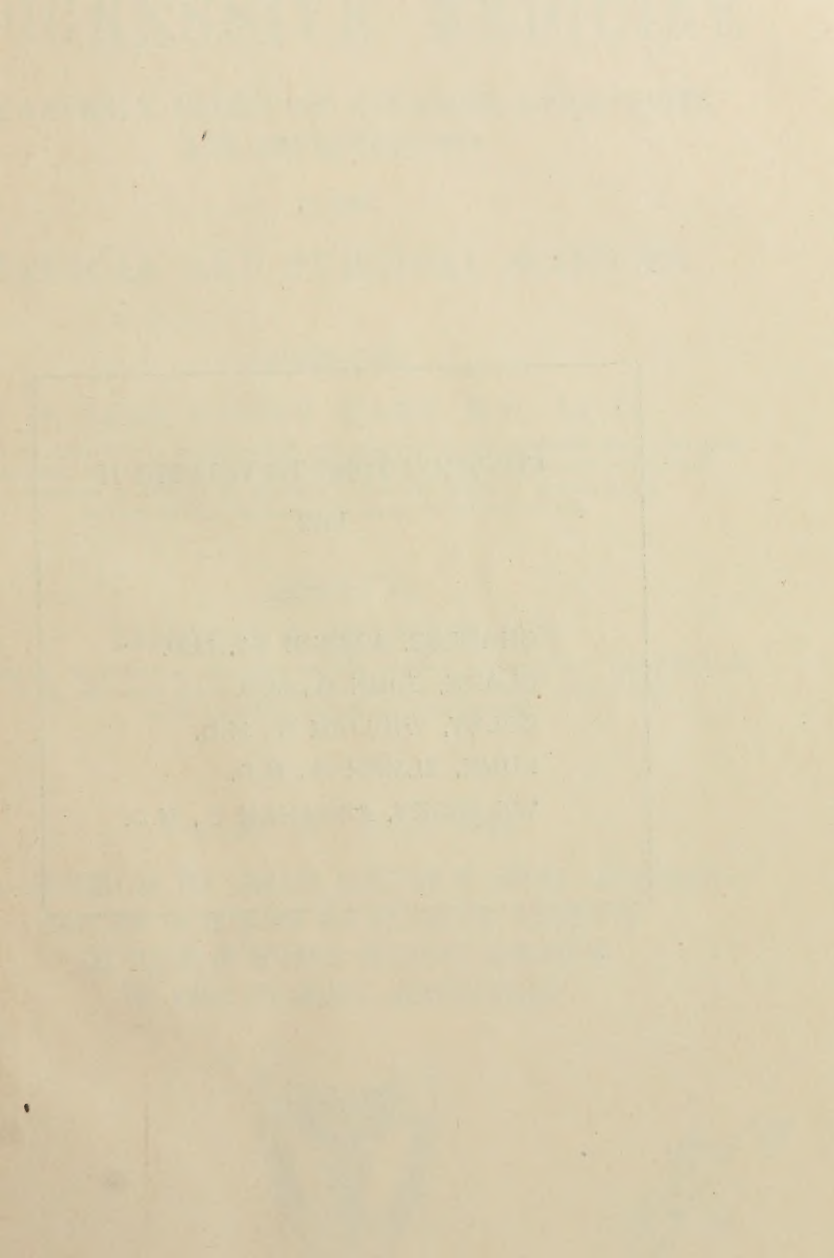
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PROGRESSIVE MEDICINE

A QUARTERLY DIGEST OF ADVANCES, DISCOVERIES AND IMPROVEMENTS

IN THE

MEDICAL AND SURGICAL SCIENCES

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HERNIA—SURGERY OF THE ABDOMEN, EXCLUSIVE OF HERNIA—GYNECOLOGY— DISORDERS OF NUTRITION AND METABOLISM; DISEASES OF THE GLANDS OF INTERNAL SECRETION; DISEASES OF THE BLOOD AND SPLEEN—OPHTHALMOLOGY
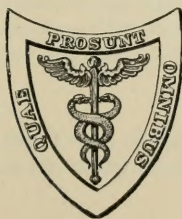
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CONTENTS OF VOLUME II

PROGRESSIVE MEDICINE.

HERNIA.

By WILLIAM B. COLEY, M.D.

Inguinal Herniotomy under Regional Anesthesia. A new method of field block has recently been published in *Surgery, Gynecology and Obstetrics* (March, 1922, page 398) by Gaston Labat of Paris, (Special Lecturer on Anesthesia, The Mayo Foundation) and William R. Meeker of Rochester, Minn. (Head of Section on Anesthesia, Division of Surgery, Mayo Clinic.)

After briefly reviewing the history of the development of local anesthesia, they show that the advance in the technic of the administration is even more striking than the improvement in anesthetic drugs. The original methods practised by Schleich, Reclus, and Halsted, consisting in peripheral intradermal infiltration and massive edematization with a dilute solution, have been gradually giving way to the more precise methods of regional anesthesia. Matas and Cushing were the first to report cases in which operation was performed by a "neuroregional" method, particularly as applied to hernia operations in which there was direct infiltration of the line of incision, and later injections of parts during operation, with special regard to making the injections in the nerve trunks at the upper outer extremity of the incision. This is the method still largely employed by surgeons who use local anesthesia in hernia. The next important step in the development of local anesthesia consisted in producing a circuminjection of the operative field in which a wall of anesthesia is made to incase or isolate the operative area, in a procedure known as field block. This principle was first practised by Hackenbruch and later popularized by Braun. Nerve blocking in herniotomy was first practised in 1911 by Laewen, who injected the nerves supplying the inguinal region at their exits from the intervertebral foramina. The authors state that nerve blocking is the procedure of choice in all work under injection methods of anesthesia. They add: "No matter how large the hernia may be, it is sufficient to inject the last three intercostal nerves and the first four lumbar nerves close to their exits from the vertebral column, a procedure known as paravertebral block. This procedure, however, is technically more difficult than regional block in which the nerves to the operative area are anesthetized farther along their course."

The authors continue: "In dealing with major operations, the successful application of regional anesthesia demands patience, time and skill, a skill that can be acquired only through practice on the human skeleton and human cadaver. . . . It is for this reason that regional or block anesthesia appeals more forcibly to the well-trained surgeon, fresh from the anatomic laboratory, at a time when his volume of operative work is small . . . Speed must be sacrificed to gentleness . . . He must be skilled in clean operative dissections and refrain from unnecessarily pulling and handling the tissues. Failure is quite likely to result if the operator is not constantly engaged in this type of work . . . The occasional operator who attempts major operations under regional anesthesia often courts failure."

As a preliminary measure, a hypodermic injection of morphine, $\frac{1}{6}$ gr., and scopolamine, $\frac{1}{300}$ gr. is recommended.

The chief advantage of regional anesthesia is its greater safety; nausea, vomiting, gaseous distention, etc., are thereby avoided. A light meal may be taken before the operation and a normal diet resumed immediately after. Stimulating drinks, like coffee, may be given immediately following. There is little, or no disturbance of the bowels, and no increase in pulse-pressure; no ill-effects on the kidneys have been noted. Anesthesia, according to their method, remains complete from one and a half hours to two hours. It avoids the edemitization of local infiltration which so often distorts the operative field. By increasing the area of anesthetization over the ordinary local method, it permits greater retraction of the tissues and greater muscular relaxation.

By creating a wall of anesthesia obliquely across the abdominal wall, passing through a point about 2.5 cm. above the medial to the anterior-superior spine of the ilium and the umbilicus, the entire nerve supply of the operative area will be cut off, with the exception of the genito-femoral and genitocrural nerves. At that level, the eleventh and twelfth thoracic nerves as well as the iliohypogastric nerve lie between the transversus abdominis and the obliquus internus muscles relatively close to the iliac crest. The ilioinguinal nerve is still in the retroperitoneal tissue beneath the transversus abdominis muscle and at about the same level as the iliohypogastric nerve. The genitocrural nerve is only accessible at the internal inguinal ring where it emerges with the spermatic cord.

The details of the technic are so important that they are given in full. *Technic:* "Unilateral reducible hernia. Anesthesia is usually induced with 100 cc of 0.5 per cent and 50 cc of 1 per cent novocaine solutions in separate containers. 10 minims of adrenalin solution 1 : 1000, are added to each 100 cc. Less solution is used for a lean patient. If the patient is very obese about 50 cc more of the 0.5 per cent solution may be required, but in the average case a total of 150 cc is never exceeded. The special regional anesthesia syringe and needles introduced by Labat (Figs. 2, 3 and 4) are employed. The patient is placed in the dorsal decubitis position and the skin prepared as for laparatomy. The operator stands on the side of the region to be anesthetized and with the smallest needle an intradermal wheal is raised at *1* about 2.5 cm.

above and medial to the anterior-superior iliac spine; this is called the parailiac wheal (Fig. 5). A second wheal is raised at *2*, which lies just about the pubic spine; this is called the pubic wheal. The subinguinal wheal at *3* lies just below the inguinal (Poupart's) ligament and lateral to the femoral artery. With a needle 8 to 10 cm. long and with an
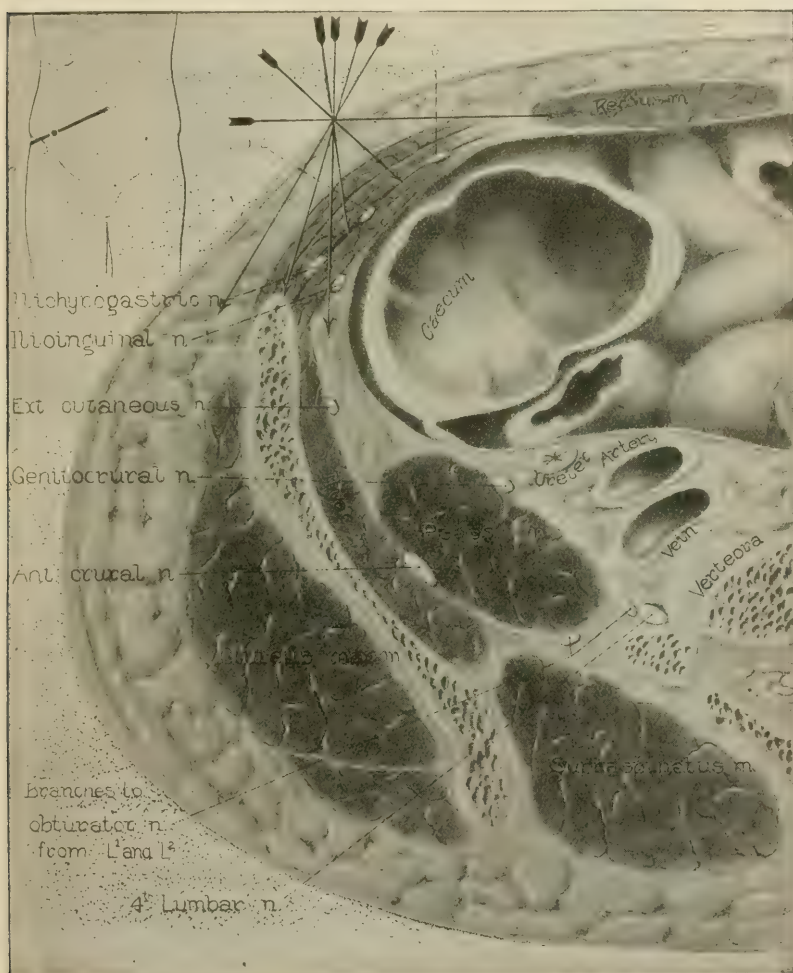
Fig. 1.—Right half of oblique cross-section of the abdomen passing through a point about 2.5 cm. above and medial to the anterior-superior spine of the ilium and umbilicus. Note the nerves and the manner of injecting through the parailiac wheal 1, in Fig. 7. (Labat and Meeker.)

equal mixture of the 0.5 and 1 per cent novocaine solutions fanwise injections are made down to the transversalis fascia in a plane perpendicular to the surface of the skin and extending from the crest of the ilium toward the umbilicus, the last injection being made just within the rectus sheath (Fig. 1). A subcutaneous injection then made in

this plane creates a wall of anesthesia which blocks the ilioinguinal, iliohypogastric, and lower two thoracic nerves. Injection should be slow, steady, and continuous as the needle advances and is withdrawn. From 50 to 60 cc of solutions is used in this injection in the average case. The needle is next introduced at the pubic wheal *2*, and deep injections into the pubic attachment of the rectus muscle on the same side are made, extending a little beyond the middle line, with about 5 cc of the
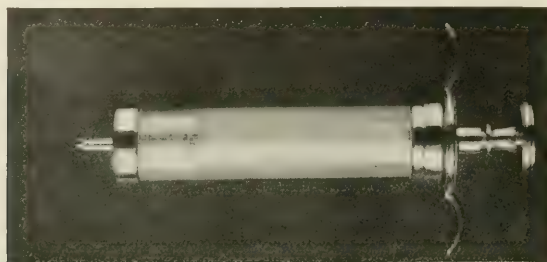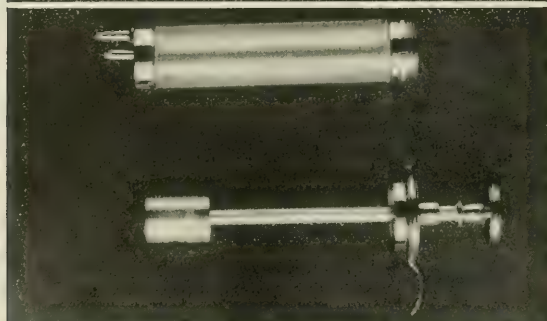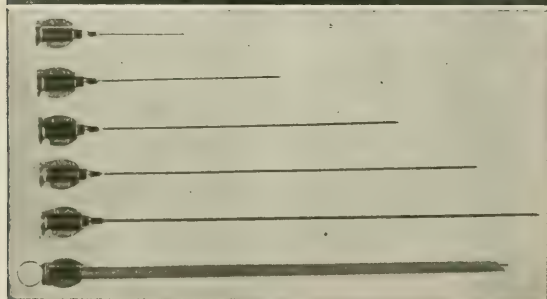
FIG. 2.—10 cc special regional anesthesia syringe.
FIG. 3.—Syringe with two parts disconnected.
FIG. 4.—Special regional anesthesia needles.   (Labat and Meeker.)

solution. Through the same wheal injections are made along the horizontal ramus of the pubis to a point 3 to 4 cm. beyond the middle line, about 5 cc of solution being employed for this also in the average case. The needle is next introduced at the subinguinal wheal *3*, deep injections are made underneath the inguinal ligament, followed by sub-cutaneous injections parallel with and along this ligament. The pur-pose of this injection is to control overlapping branches coming from

the anterior crural and external cutaneous nerves and permit greater pull on the inguinal ligament in the approximation of the deep layers. About 10 cc of the 0.5 per cent solution is needed for this.
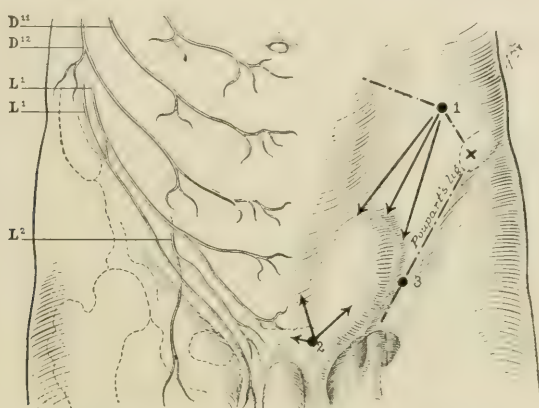
Fig. 5.—Left inguinal field block for reducible hernia. *x*, anterior-superior iliac-spine; 1, parailiac spine; 2, pubic wheal; 3, subinguinal wheal. Note nerve distribution on the right side. (Labat and Meeker.)

"If the hernia reduces spontaneously in the supine position, or if reduction maintains after taxis, the cord structures are next grasped between the thumb and index finger of the left hand at the external ring, or at the point the cord crosses the pubis, and the needle inserted through the pubic wheal. The position of the operator for the injection
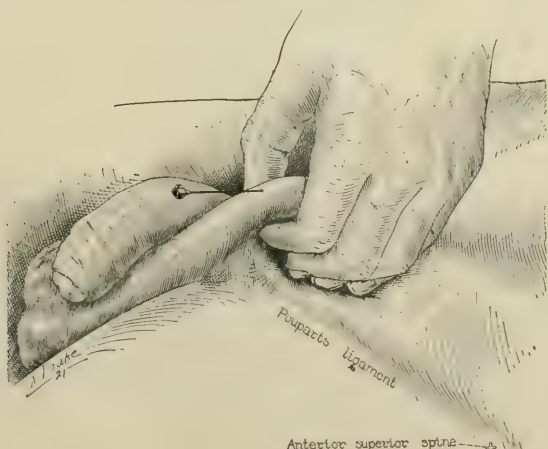
Fig. 6.—Manner of injecting the cord while maintaining reduction with the last three fingers of the left hand. (Labat and Meeker.)

of the cord depends on the side to be injected, the injection being best made from the pubic spine upward. The cord structures are transfixed and injected with about 5 cc of the 1 per cent solution, care being

exercised not to traumatize the cord structures by multiple punctures, causing hematomata, which, however, are of no clinical importance. The cord is then massaged a little so as to hasten the diffusion of the solution.

"The last injections are at the margins of the internal ring. If the internal ring is easily found by the palpating finger, the needle is advanced from the pubic wheal in the subcutaneous tissue to a point just medial to the margin of the ring. The fascia is then perforated at this point and the injection made. Similar injections are made above and lateral to the margins of the internal ring, 5 to 10 cc of the 1 per cent solution being used. If the internal ring cannot be located by palpation, the injections are made midway between the pubic and anterior-superior iliac spines about 2.5 cm. above the inguinal ligament. These injections surround the neck of the sac and are meant for blocking the genito-femoral nerve, but failure to anesthetize this nerve occasionally happens, thus necessitating its injection after exposure of the cord.
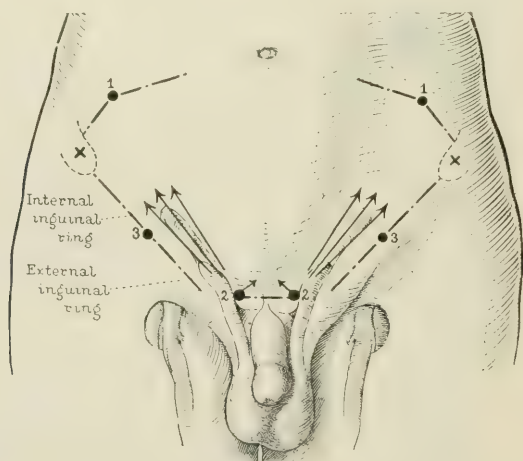
Fig. 7.—Bilateral inguinal field block. (Labat and Meeker.)

"Occasionally the reduction of the hernia is not maintained of itself, even with the patient in the supine position, the mass reappearing as soon as the pressure is released. In such cases reduction is maintained with the last three fingers of the left hand while the cord is grasped with the thumb and forefinger and injected as previously described (Fig. 6). The injections around the internal ring are here best made from above the parailiac wheal in order to prevent a possible puncture of the sac and its contents.

"*Bilateral reducible hernia.* Fig. 7 illustrates the bilateral block which is based on the principles described for unilateral herniotomy. The quantity of solution is 200 cc of the 0.5 per cent and 50 cc of the 1 per cent, with 20 drops of adrenalin in all."

Labat and Meeker believe that, while a little more time is required for regional anesthesia than for general anesthesia, the advantages of

the former are sufficient to compensate for any loss of time. They believe there are no contraindications for regional anesthesia except in very young patients.

In conclusion, they state that regional anesthesia with novocaine-adrenalin solution is the method of choice in inguinal herniotomy and should be used generally instead of only for patients who are unsafe subjects for general anesthesia.

While we have performed a considerable number of operations for all types of hernia under local anesthesia, using the older method of infiltration and injecting the nerves when exposed, we have never tried the method herein described. We have found little difficulty in obtaining more perfect anesthesia by the older method, and ideal end-results have
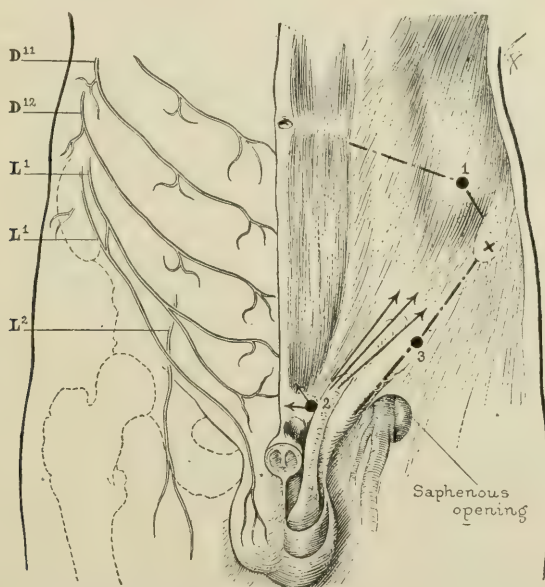
Fig. 8.—Inguinal field block for irreducible inguinal herniotomy. 1, parailiac wheal; 2, pubic wheal; 3, subinguinal wheal. Note injections of the internal ring from the parailiac wheal. (Labat and Meeker.)

followed. We have, however, limited the local anesthesia to adults, in whom there were some contraindications for general anesthesia, or who had some antipathy toward taking the general anesthetic. We believe that the field of local anesthesia in inguinal herniotomy has been greatly enlarged and that, in the not distant future the majority of cases of uncomplicated hernia will be done under local anesthesia. Strangulated hernia should practically always be operated on under local anesthesia. We doubt if it would be possible or wise to extend regional anesthesia to young children. Gas oxygen or gas ether in young children is so seldom followed by complications, in operations which can usually be performed by anyone familar with the technic in eight or ten minutes, that we still regard it as the method of choice.

New Methods. Of all the *new methods of operating for the radical cure of hernia*, in recent years, we believe that of W. E. Gallie and A. B. LeMesurier, of Toronto,[1] is, perhaps, the most important.

This method is intended by the authors to be used only in very large direct hernia or large recurrent hernia, in which it is difficult to find sufficient muscle or fascia to permit satisfactory closure of the opening. The method is based upon the use of living sutures in operative surgery, a method which is, we believe, original and may be applied to many other conditions than that of hernia. In a way, it is somewhat similar to the method reported by MacArthur, of Chicago, many years ago, in which he used for sutures strips of fascia from the aponeurosis to close the hernial opening, leaving the proximal end of the suture attached at the base. A careful study of the literature shows that autogenous transplantation of tendon and fascia has been frequently employed clinically, and the method has also been closely studied in the laboratory. Dean Lewis, of Chicago, proved that the tendinous fasciæ could be transplanted to another position in the same animal and that such transplants would retain their normal gross and histologic characteristics. He applied this principle in filling in gaps in tendons and in making fascial sheaths to protect the point of suture of severed nerves. Gallie and LeMesurier first repeated the experiments of Lewis and then carried on three series of experiments. In all of these an observation was made which they regarded as of utmost clinical importance, this was, that neither in fascia, aponeurosis, nor tendon is there any evidence of proliferation of the essential cells of the tissue. When healing occurs, therefore, the connective tissue which forms at the point of union arises from cells which are not tendon cells, and which cannot be expected to produce true tendinous tissue, but simply produces an ordinary scar which later on stretches, and in this fact lies the explanation of the failure to cure large hernias by the use of patch transplants and also to bridge gaps in damaged tendons by end-to-end sutures of transplants of tendon or fascia.

Gallie and LeMesurier believed that the method of transplantation of tendinous tissue would be of little clinical value until some means had been discovered of securing a firm union of the transplant to the surrounding structures. With this object in view, they undertook a series of experiments in which a piece of fascia one-quarter of an inch wide and two inches long was removed from the back of an animal, and then passed transversely across the middle of the gap and woven two or three times into its edges (Fig. 9). These experiments were repeated, substituting free transplants of aponeurosis and tendon instead of fascia. The results showed that the solidity of the union of the transplanted fascia to the edges of the gap depended on the extent to which the former was woven into the latter. If the transplant passed only once or twice through the fascial margins, it usually failed to prevent the edges of the gap from stretching apart. Gallie and LeMesurier state, that: "The strength of the union also depended on the care with which the portion

of the fascia used in the weaving was cleared of areolar tissue. Actual scraping and scarification of this part of the transplant produced the best results. Examination of the points of contact of the transplant and the surrounding fascia showed that the union occurred by means of new-formed connective tissue which ranged from the loose texture of areolar tissue to the firmness of ordinary scar. It is evident, therefore, in order that the union may be strong enough to stand the normal physiologic strain, that the transplant must be in actual contact with its bed over a considerable distance.

"In many operations, however, such as the repairing of the gaps in the fascia of the rabbit's back, the weaving of the transplant into the edges of the gap and anchoring it with catgut sutures is too laborious and uncertain a procedure to make it applicable to ordinary operative surgery. The search for a method of overcoming this difficulty finally led to the idea of using long strips of fascia and threading them on large-eyed needles, thus converting the transplants into living sutures. The idea was immediately tested experimentally and has proved to
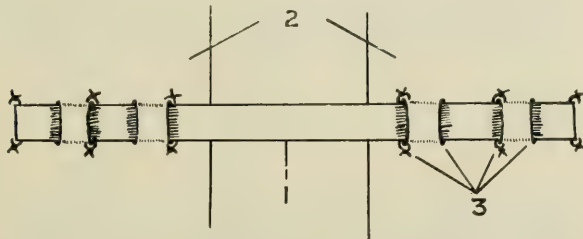
Fig. 9.—Diagram showing method of fixation of "strip" transplant by weaving through slits in the fascia on either side of the gap. 1, "strip" transplant; 2, edges of gap in fascia; 3, slits through which strip is woven and fixed by sutures. (Gallie and LeMesurier.)

be the most valuable result of our research. In these experiments a strip of fascia, a quarter of an inch wide and six or seven inches long, was removed from the animal's back and threaded into a needle (Fig. 10). It was found necessary to tie the fascia into the needle, as it is so slippery that it will otherwise constantly slide out of the eye. A catgut ligature was also tied about the terminal end of the fascial suture to prevent splitting. The needle was now passed through one of the edges of the fascial gap and then through the terminal end of the living suture and the suture drawn taut. The needle was again passed through the edge of the fascia and also through the fascial suture to make doubly sure that the anchor would hold. The needle was then carried across the gap in the fascia and passed through the end of the opposite side. When the suture had been drawn taut, the needle was either passed through the suture and again through the edge of the gap, or was passed through the edge of the gap and then looped so as to anchor the suture by a knot in itself.

"The specimens were recovered at intervals of one week up to a little over a year. They show that the fascial sutures behave in practically

the same way as the transplants in the first series of experiments. There is the same early inflammatory dilatation of the neighboring blood-vessels and the formation of a film of exudate over the whole operative field. Soon minute bloodvessels can be seen spreading through this film on the surface of the suture. As the suture presents a folded appearance on cross-section, the film of exudate, which later becomes areolar tissue, extends into the spaces between the folds of fascia, bringing bloodvessels into contact with all its surfaces (Figs. 11 and 12).
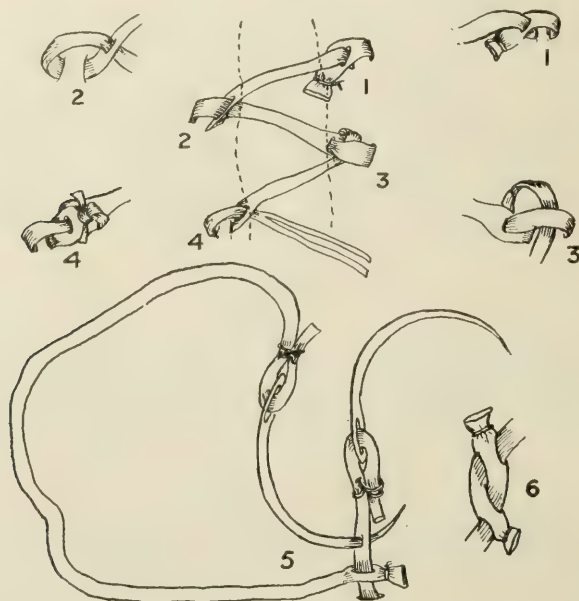
Fig. 10.—Diagram showing method of inserting fascial suture. 1, anchoring suture at commencement by looping it through itself; 2, fixation of suture at each loop by passing it through itself; 3, fixation by passing suture through itself and tying in knot; 4, ending of suture by passing through itself, splitting, and tying ends in knot; 5, method of joining new suture to one that has been inserted; 6, join completed. (Gallie and LeMesurier.)

"These experiments conclusively demonstrated the clinical value of the principle of the use of living sutures. The edges of the gap in the fascia were solidly held together as at the time of the operation. The suture had healed to the edges at all the points of transfixion, and the loop and knots had become reduced to small nodules of fibrous tissue. At no point had the suture cut out or become loosened, nor was there any evidence of stretching or contracture of the suture itself. This latter observation was amply proved in a series of experiments in which black silk markers were tied on the suture at accurately measured intervals. When the specimens were recovered these markers were always at practically the same distance from one another. Further, in no case had rupture of the suture occurred. Even in rabbits the strips of fascia are very strong, stronger than ordinary number two

catgut, and strips of human fascia lata, which is the material we have
used in surgical operations, are stronger than the stoutest kangaroo
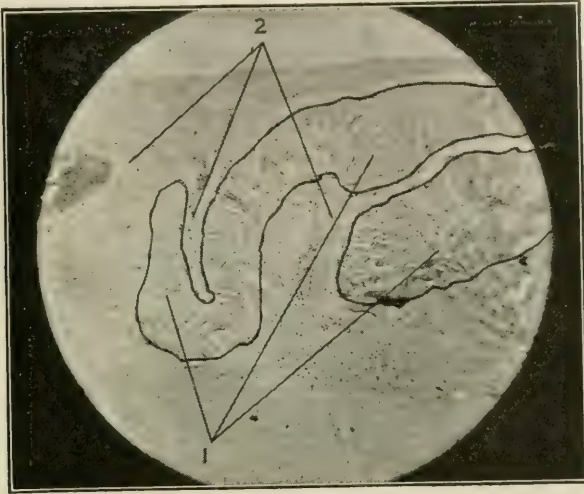
FIG. 11.—Cross-section of portion of fascial suture after three weeks (low power).
1, folds of fascia; 2, new-formed vascular tissue surrounding whole suture and
extending into spaces between fascial folds. (Gallie and LeMesurier.)
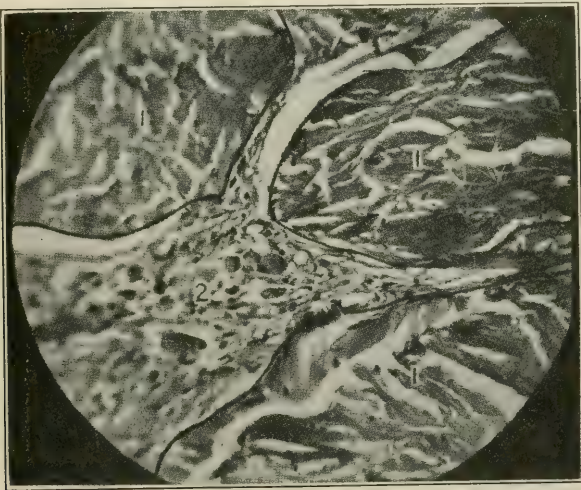
FIG. 12.—Same as Fig. 10, but under high power. 1, folds of fascia; 2, new tissue
between folds. The cells of the fascia are staining well, the outline of each fold is
distinct, and there is no invasion of the fascia itself by the new tissue. (Gallie and
LeMesurier.)

tendon. Destruction of the normal blood supply and transplantation
to another position in the body appears to have no effect on the strength
of the suture."

After discussing the numerous conditions found in general and orthopedic surgery in which the method can be used to great advantage, Gallie and LeMesurier describe in some detail its application to hernia. They call attention to the fact that the published records of all well-known clinics show that the number of recurrences after the operative treatment of large ventral hernias, direct inguinal hernias, and old oblique hernias in patients past middle age, is most unsatisfactorily high, and they have great hope that the use of this principle of living sutures will materially improve the results in these varieties of hernia.

In conclusion, Gallie and LeMesurier state: "Up to date we have operated on 30 patients. A few of these were suffering from recently acquired direct inguinal hernia but the majority were cases of recurred direct or indirect inguinal hernia, or supposedly inoperable ventral hernia. There was 1 case of recent indirect inguinal hernia in a man suffering from a complete flaccid paralysis of the abdominal muscles. Beyond the removal of the sacs, the treatment in these cases consisted of repairing the weak abdominal wall with living sutures of fascia lata. These sutures were about seven inches long and a quarter of an inch wide. They were threaded upon a curved large-eyed needle and woven into the edges of the surrounding muscles and aponeurosis much as one darns a sock. No attempt was made to drag the structures into which they were woven out of their normal positions, as is so frequently done in the ordinary operations, but simply sufficient tension employed to make the suture lie flat. Thus the success of the operation depends not upon inducing such structures as the internal oblique muscle or the conjoined tendon to heal to Poupart's ligament, but solely upon the strength of the living suture and upon its firm grip of the surrounding tissues. One case serves to illustrate the value of the method. A soldier was admitted to hospital with a huge ventral hernia resulting from a shell wound which tore away the right upper portion of the abdominal wall, including most of the rectus muscle. When we saw him he had a hernial ring of oval shape which measured seven inches by four. All who saw him agreed that by ordinary methods one could not hope for a cure. Our operation consisted of the removal of the scar and sac, the exposure of the edges of the muscular and aponeurotic ring and the closure of the opening by layers of living sutures which were woven strongly into the surrounding structures and crossed each other as in the weaving of a basket. The result has been most gratifying. As you see the hernia is cured and the abdominal wall is as firm as could be desired.

"These operations for hernia have now extended over a period of nearly two years and, up to the present, there has not been a single recurrence. One of the cases suppurated mildly, but after discharging pus for about four weeks healed up without extrusion of the sutures and has remained solid ever since. When one considers that these were all difficult cases, many of which had been operated upon once or twice previously, by first-class surgeons, the value of the principle of living sutures must be apparent. We believe that we have found a method

which will reduce the percentage of recurrences to a negligible quantity and greatly widen the field in which operative interference will be of value."

During the meeting of the American Surgical Association in Toronto last June, I had an opportuunity of seeing Gallie perform one of these operations. I was greatly impressed with the value of the method, and particularly, with Gallie's ingenuity and skill in applying the sutures. The fact that no recurrence has as yet developed in 30 cases treated over a period of two years, gives added hope that the method will prove of great value in that type of operation in which it has been hitherto most difficult to secure permanent cure.

Among the more important newer methods brought out during the last year is one described by Pitzman of St. Louis, Mo.,[1] entitled, "*A Fundamentally new Technic for Inguinal Herniotomy.*"
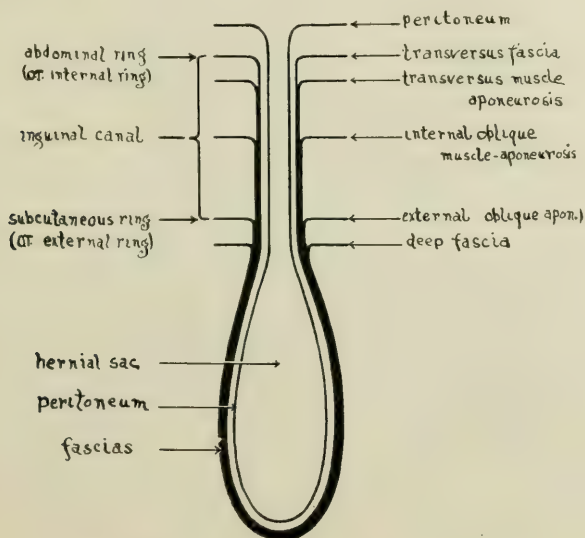
FIG. 13.—Diagram of inguinal hernia. (Pitzman.)

Pitzman states, that beyond reasonable doubt, the Bassini operation marked the turning-point in the history of inguinal herniotomy for it was only after his report that we are justified in speaking of radical cures. Pitzman believes that the most important part of the Bassini operation was resection of the inguinal canal portion of the hernial sac, as prior to that time, operators had rarely ever made a complete removal of the sac. Nearly all of the various procedures which have been introduced since Bassini's report, have made use of this important step. Pitzman believes that the very high percentage of cures obtained by Kocher's method—nearly equaling that of Bassini's—was due to the fact that his method accomplished complete closure of the sac, although in a more complicated and less satisfactory manner

[1] Annals of Surgery, November, 1921, p. 610.

than that obtained by the Bassini method. According to Pitzman, "While the original Bassini technic and the Bassini modified to bring the internal oblique and transversus muscles in front of the cord still have many adherents, the strong tendency throughout the world during later years has been to reinforce these muscles by flaps from the external oblique aponeurosis," according to the technic of Andrews of this country and Girard, of Europe.

Believing that anatomy forms the foundation on which every herniotomy must depend, Pitzman has made a very careful study of the anatomy of the inguinal canal.
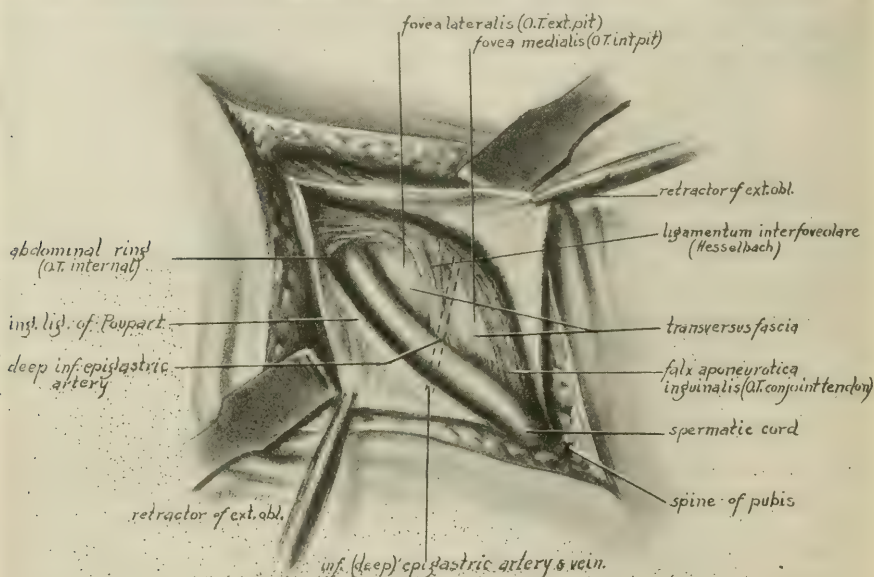
FIG. 14.—Anatomy of inguinal region (extra-fascial fat removed). (Pitzman.)

According to Pitzman, the essential fact is "That the whole area between the inferior margin of the transversus muscle and the inguinal ligament of Poupart is protected by the transversus fascia, reinforced throughout most of its extent by broad sheets of aponeurosis. The only anatomic opening is where the cord (funiculus spermaticus) pierces the transversus fascia and this is reinforced at its danger point, inferiomedially, by the inferior portion of the ligamentum interfoveolare.

"All anatomies, so far as noted, stressed the importance and strength of this transversus fascia and the overlying aponeurosis layers. Most of the surgical discussions on the other hand simply mention this fused layer mechanically, without laying one particle of stress on it, or even go to the extreme with Pólyá[1] who after a very complicated description

[1] Arch. f. klin. Chir., 1912, **109**, 816–877.

states its strength is not worth considering. Which brings us to the question of which group are correct and how this difference of opinion came about? I believe the anatomists are correct in their description of what they are much more familiar with, *i. e.*, the normal status, while those surgeons who do not admit it has any particular strength are describing the abnormal, *i. e.*, when the layer has become atrophied under continued pressure of a very large hernia, or more particularly when it has been damaged by a previous operation. I agree emphatically with the anatomists that this fused aponeurosis fascia layer is functionally the essential factor in keeping the intestines from entering the
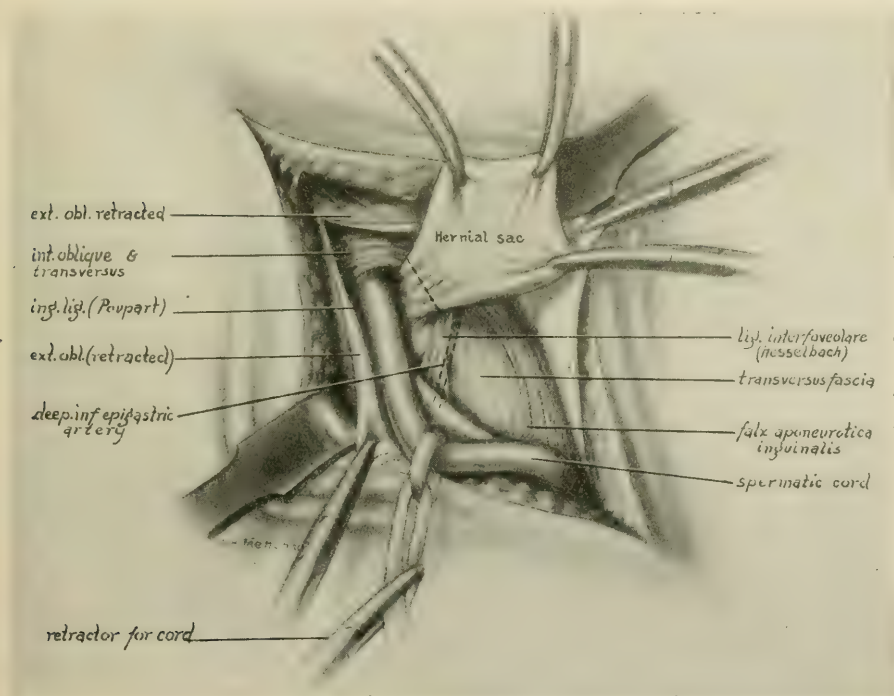
FIG. 15.—Separation of hernial sac. (Pitzman.)

inguinal canal. The fact is, this layer is sufficiently strong in practically all individuals to prevent hernias from really entering the inguinal canal, except at its point of least resistance along the spermatic cord. In my dissecting room tests of the 6 bellies opened this year, I could not push my gloved finger through the transversus fascia aponeurosis at any point, except directly against the spermatic cord. Genuine direct hernias are simply a relaxation and bulging outward of this layer, and practically never form a true sac or enter the scrotum.[1] This is popularly very much misunderstood because many surgeons diagnose very

[1] See Moschcowitz's discussion, In Johnson's Operative Therapeusis, Appleton & Co., 1915, p. 42.

large-necked hernia, which from its nature extends down close to the lateral margin of the rectus muscle as direct. On the other-hand, fully half of the hernia recurrences are direct, but this only shows that after our usual herniotomy technics this layer is no longer strong and resistant—a proposition I will discuss in more detail later. For those surgeons still skeptical about the normal strength of this fascia aponeurosis sheet, a simple test in their next small or medium-sized herniotomy would be to put their index finger through the neck of the hernial sac into the belly cavity and then press forward against the layer. On their conclusion from this test I am willing to rest this anatomic discussion of the posterior wall of the inguinal canal.''

opening into peritoneal cavity

deep epigastric artery

ext. obl. aponeurosis

resection line neck of sac

lig. interfoveolare

transversus fascia o medial fovea

Falx aponeurotica inguinalis

ext. obl. aponeurosis
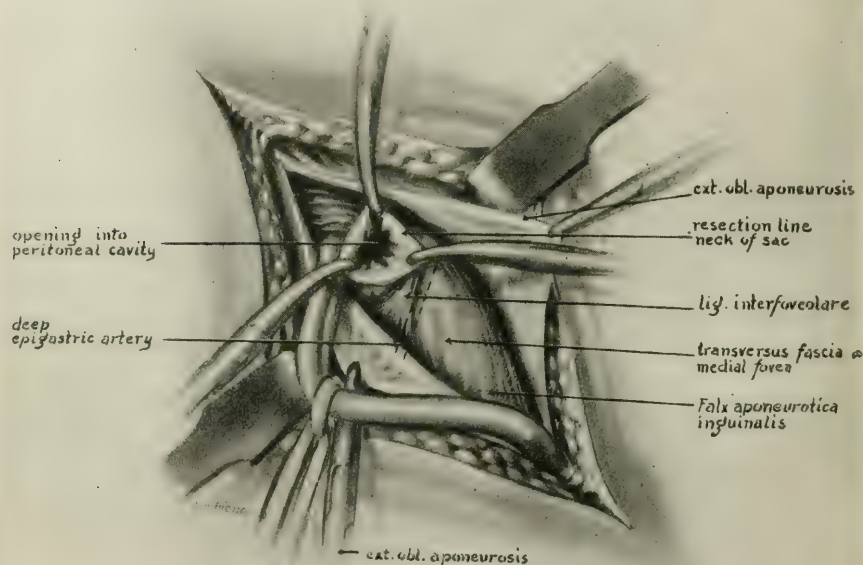
FIG. 16.—Resection of hernial sac. (Pitzman.)

Pitzman states that he worked out the theory of his operation on precisely the same basis as Bassini.[1] To quote the latter:

"I thought to myself that this could be worked out by means of the rebuilding of the hernial canal, as this exists under physiologic conditions, that is, a canal with two openings, an abdominal and a subcutaneous, further with two walls, a front and a back through the middle of which the spermatic cord would run obliquely." In discussing the physiologic anatomy of the canal, later on, he states, "In order to make possible the radical cure of inguinal hernia, it is, accord-

[1] Arch. f. klin. Chir., vol. 40, p. 435.

ing to my contentions, indispensable that the original physiologic (valve) type of the inguinal canal be reproduced."

While Pitzman believes that Bassini grasped the essence of the problem, in applying his theory to practice, Pitzman is of the opinion that he made a grievous mistake, which chanced to swing the tide of all effort in the wrong direction. He continues, "Bassini split the aponeurosis of the external oblique, separated out the hernial sac and then tied off the neck of the sac. Everybody followed suit. In justice to Bassini, let me call attention to the fact that on account of the danger of peritonitis during that stage of surgery, most operators refused even to open the hernial sac, using various torsion methods instead. His
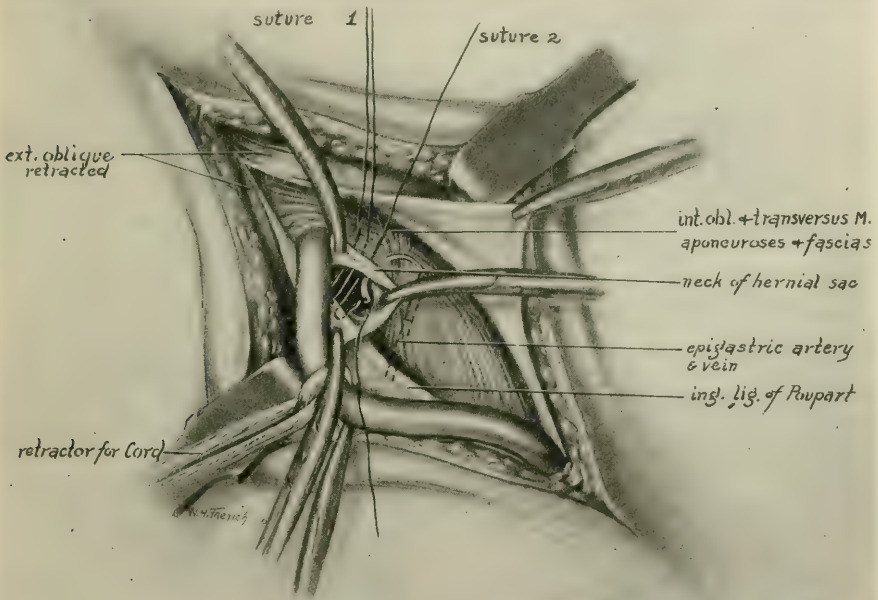
FIG. 17.—Insertion of interrupted sutures. (Pitzman.)

opening of the sac was a progressive step forward, and he was probably, subconsciously at least, influenced by his anxiety to close off the peritoneal cavity at the earliest possible moment. Bassini then resected the inguinal canal portion of the sac and proceeded to attempt to repair the abdominal ring and posterior wall of the inguinal canal. He aimed to sew the musculus obliquus internus, the musculus transversus and the fascia verticalis Cooperi (old name for transversus fascia and aponeurosis) down to the inguinal ligament of Poupart. But let me quote *verbatim*, page 437: 'For the just discussed suture it is advisable to use silk and interrupted sutures, and to take hold of the threeply musculo-aponeurotic layer at 2 to 3 cm. from its (lower) edge. The lower two stitches—into lateral margin of rectus.'"

3

Pitzman asks, "By what anatomic authority sew the internal oblique and transversus muscles down to the ligament of Poupart? As Bassini quotes none and it is not even mentioned among the occasional anatomic variations in reference volumes, I feel confident that he fell short of his own theory. That is why I feel he made a mistake, which has been universally followed. All of which refers purely to the physiologic anatomy of the canal, and is entirely aside from the question as to whether sewing these muscles down to the inguinal ligament of Poupart will yield a larger percentage of permanent cures. In my judgment, Bassini was right in maintaining he did not transplant the cord but
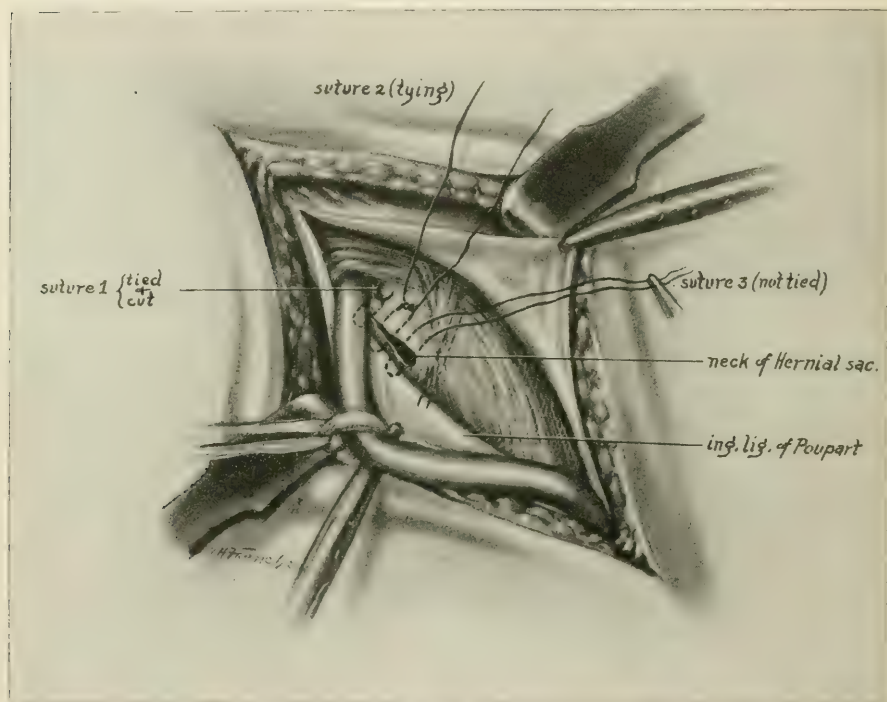
FIG. 18.—Tying of sutures.   (Pitzman.)

he did transplant the muscles, at least temporarily. These statements apply, in my judgment, with equal force to the so-called anatomic modification, which consists in sewing the internal oblique and transversus muscles down to the inguinal ligament superficial to the cord. Bassini unquestionably aimed and thought that he had also sewn the transversus fascia and aponeurosis down to the inguinal ligament, but it is doubtful whether he ever really accomplished that object in even a small minority of his cases. With no protection for the intestines and with the peritoneal cavity closed, only a foolhardy surgeon would ever really catch the transversus fascia in even a single stitch. The fact is, most modern authors concede that they catch only the internal

oblique and transversus muscles in their stitches. From the physiologic anatomy basis Bassini was therefore doubly wrong, as he caught the layer he had no warrant for catching and missed the layer he should have caught."

We believe Pitzman's objections to the Bassini method are purely theoretical and have little basis in actual fact. Whether Bassini missed the layer he should have caught, or caught the layer he should have missed, may be interesting from the standpoint of "physiologic anatomy," but, in our opinion, the point of far greater importance is, that radical and permanent cure of hernia has been accomplished by Bassini's method. Our statistics at the Hospital for Ruptured and
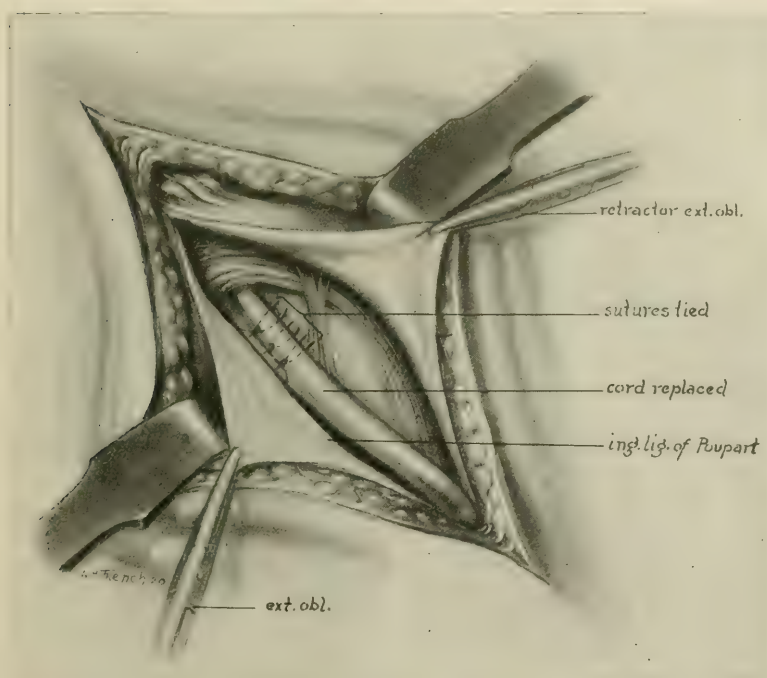
Fig. 19.—Replacement of cord. (Pitzman.)

Crippled since 1890, covering nearly 10,000 cases in which a careful follow-up system has been carried out during the entire period, show beyond any doubt whatever, that Bassini's method without essential modifications has been able to effect a permanent cure in 98 to 99 per cent of cases of indirect inguinal hernia.

Pitzman failed to find a single reference in the literature on the very important question as to whether, in a satisfactorily healed hernia, the internal oblique and transversus muscles usually remain strongly united to the inguinal ligament and functionally capable. Whatever may be the theoretical reasons advanced, and there have been many repeatedly advanced, that the internal oblique muscle will not unite

firmly with Poupart's ligament, the effective answer is, that it does.
We have operated on a sufficient number of relapsed cases at the Hospital
for Ruptured and Crippled and other hospitals, to prove this point
beyond any doubt. In some of these cases the original method of
operation employed has been the Halsted, and, in some, the Bassini
in which the suture which we have long used above the cord, had not
been employed and a recurrence took place at the site of the internal
inguinal ring; we found the internal oblique firmly united to Poupart's
ligament nearly down to the pubic bone. In some of these cases, the
original operation was performed more than ten years prior to the
second. These practical observations outweigh any amount of theory.
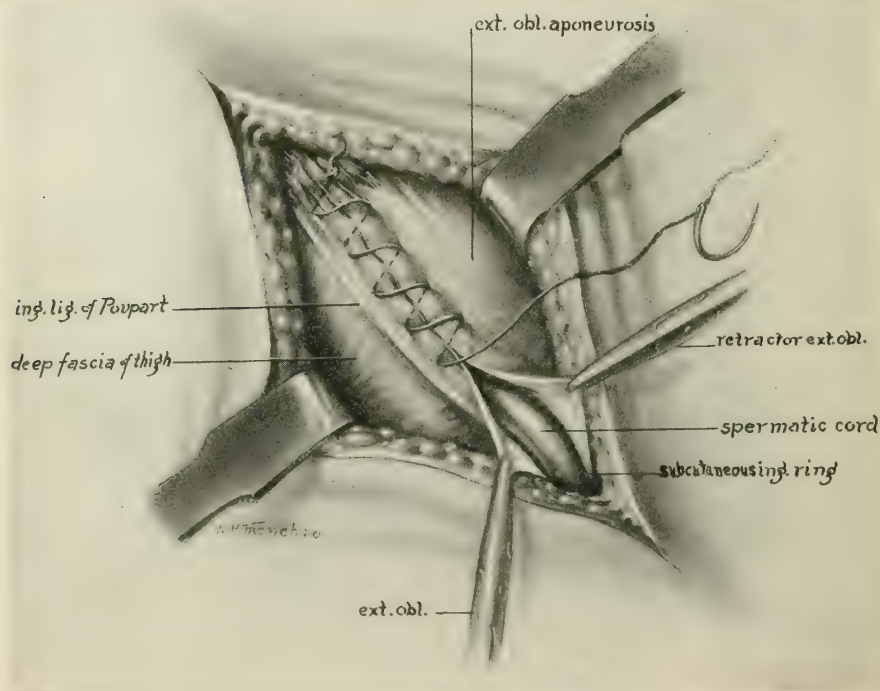
Fig. 20.—Suture of ext. oblique aponeurosis.   (Pitzman.)

Pitzman's operation, which is very well shown by the excellent
illustrations accompanying his article, is practically the Bassini oper-
ation without the suturing of the internal oblique and transversus
muscles to Poupart's ligament. It consists in suturing, instead of tying
off the sac high up in the order of Bassini's operation; three or four or
more mattress sutures pass through the neck of the sac including the
transversus muscle fascia on the inner side and Poupart's ligament on
the outer. These sutures not only close off the sac high up but bring
the aponeurosis, fascia and muscle, into apposition with Poupart's
ligament. If this is done, Pitzman believes that the suturing of the

internal oblique to Poupart's ligament is entirely unnecessary. While this may be quite true in many cases of hernia in children and in adults with small sacs, we do not believe it should take the place of the Bassini operation for routine cases. Pitzman's main objection to the Bassini operation, that the internal oblique does not remain firmly attached to Poupart's ligament, is, in our opinion, based entirely on theoretical reasons which have been proven by actual observation to be unsound.

Pitzman, in closing, states that he does not attempt to give statistics of a recent limited series, believing that the value or lack of value of any technic can only be determined by the results of other than the originators.

In his summary of conclusions, Pitzman, gives a reason so often advanced in the introduction of new methods, viz., that, the "Size and endlessness of the stream of inguinal herniotomy technic raises the strong suspicion that something is fundamentally wrong."

We, personally, cannot feel that there is anything very fundamentally wrong with the Bassini method in view of the results obtained at the Hospital for Ruptured and Crippled, and many other clinics. Also, we do not agree with him further on in his summary that "this technic is universally applicable to all inguinal hernia, small or large, direct or indirect, primary or recurrent; especially advocated for medium and large-necked hernias." We do not believe it at all applicable for large direct inguinal hernia. The main idea of Pitzman's operation, *i. e.*, insertion of the sutures so as to include the transversus fascia and the peritoneum of the neck of the sac, to within one-eighth to one-quarter inch from the edge of Poupart's ligament, by mattress sutures, may possibly have some advantage over the ordinary high ligation of the sac or transfixation, but that this would enable us to do away entirely with the suture of the internal oblique to Poupart's ligament, we believe is far from proved.

Skillern,[1] of Philadelphia, in discussing the choice of operation in inguinal hernia, points out that the type of sac is a determining factor in whether the posterior wall is in need of reconstruction or not.

What he characterises as a "stalk sac" is a long, narrow, thin, empty, non-adherent sac, representing an unobliterated funicular process encountered in early life, adolescense, as well as in recent hernia in well-muscled adults. In such cases he believes that high ligation of the sac without reconstruction of the posterior wall is sufficient to effect a cure. The "sessile sac" on the other hand, which is confined to a direct sac, he states, need not be ligated, merely turned in, but reconstruction of the defective posterior wall is the essential factor in this type.

The important features of the operation which Skillern advocates are, "free exposure and thorough cleaning of Poupart's ligament, Gimbernat's ligament, the triangular fascia, the pubic head of the rectus enclosed in the linea semilunaris, the linea semilunaris itself and the aponeurosis extending laterally from it; firm reconstruction

[2] Surgery, Gynecology and Obstetrics, February, 1922, p. 230.

obtained by developing a finger-like cylinder of the musculo-aponeurotic
tissue just mesial to and above the thinned-out conjoined tendon and
internal oblique muscle fibers, suturing this cylinder to Gimbernat's and
Poupart's ligaments from the pubic bone to beyond the internal ring,
fastening the lower flap of external oblique aponeurosis down the
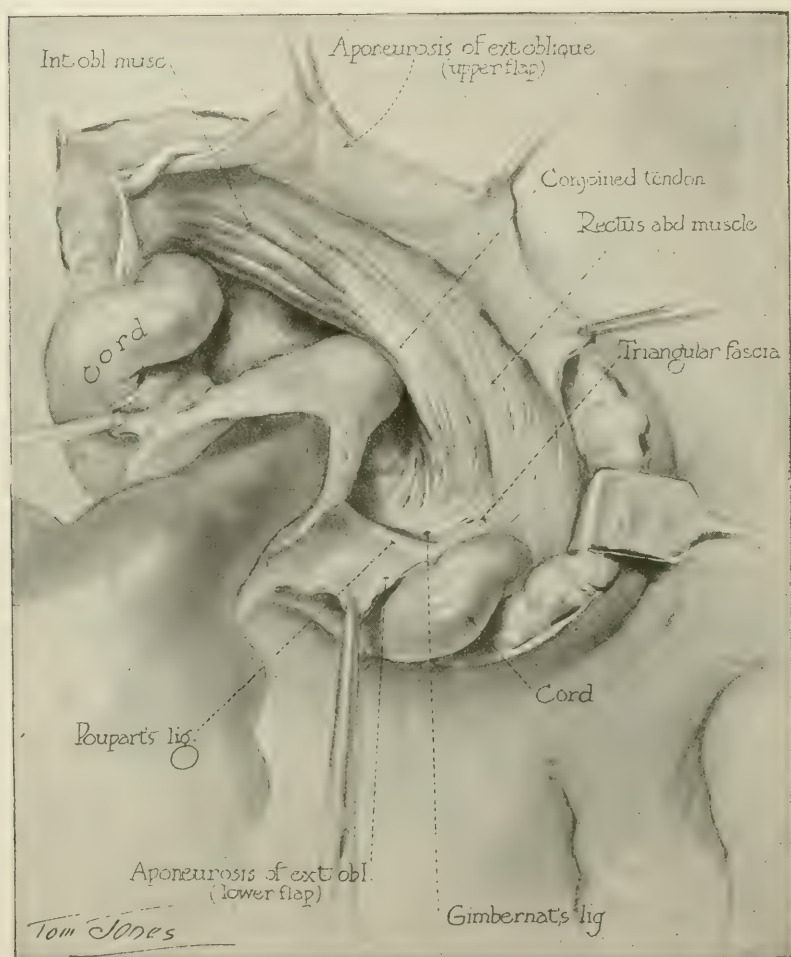
FIG. 21.—Inguinal canal laid open, cord retracted, gauze-covered index placed in
hernia (inguinal) triangle and pushed against lower border of conjoined tendon
until there develops a stout, finger-like cylinder of aponeurosis-covered musculature
which is to be sutured to Gimbernat's and Poupart's ligaments.   (Skillern.)

cylinder and the upper flap down upon the lower, thus imbricating the
two flaps and taking the strain away from the first row of sutures;
bringing the cord out somewhat lateral to the internal ring, prevent-
ing constriction of it and transposing it to the surface of the imbri-
cated external oblique flaps; and finally obliteration of dead spaces by
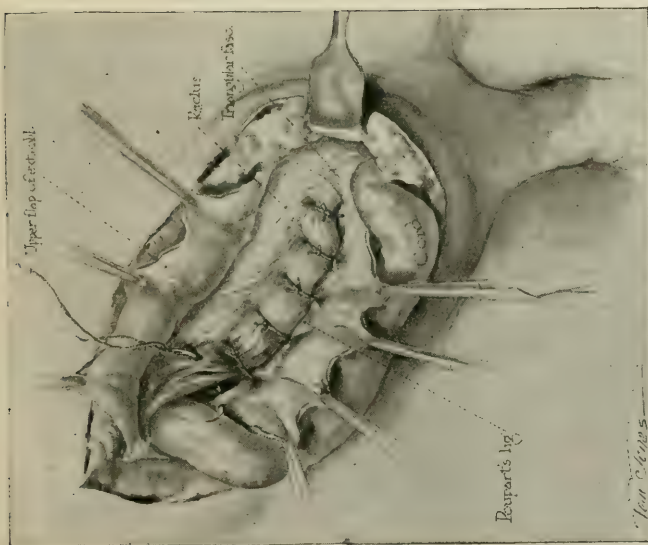
Fig. 22.—The stout, finger-like cylinder is sutured to Gimbernat's, then to Poupart's ligament, using interrupted sutures of No. 2 chromic gut, doubled and carried by a small, full-curved, non-cutting needle. The innermost suture is inserted just to the outer side of the triangular fascia into the lowermost portion of the linea semilunaris, including in its bite a thickness of the aponeurosis-covered rectus head about equal to that of the little finger, and below, an area of Gimbernat's ligament of corresponding breadth. The remaining sutures are passed in the same manner until the cord is reached, the tissues included in their bite varying in name, but not essentially in structure, although the outermost usually encounters muscle tissue of internal oblique instead of aponeurosis. (Skillern.)

Fig. 23.—Interrupted sutures of single-thread No. 2 chromic catgut tack lower flap of external oblique aponeurosis down upon finger-like cylinder. The innermost passes close to outer pillar of external ring. Each stitch takes in its bite a portion of the cylinder situated between two deep sutures. A nick for the passage of the cord is made in the lower flap beyond the last suture. The effect of this row is to grip the cylinder and retain it in contact with Gimbernat's and Poupart's. (Skillern.)
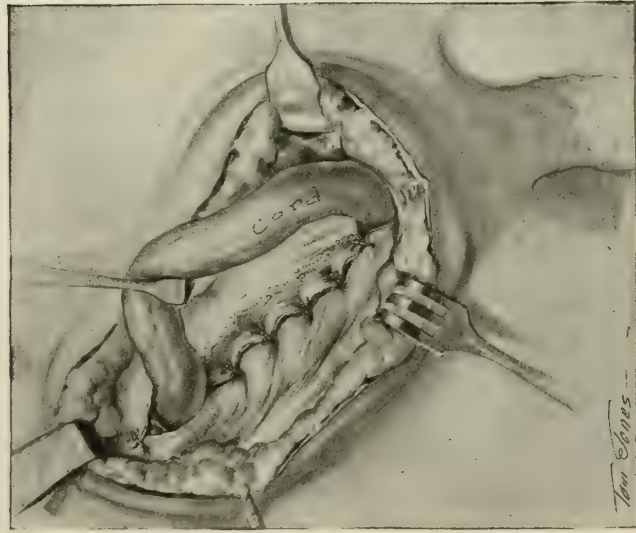
Fig. 24.—The upper flap of external oblique aponeurosis is tacked down upon the lower flap, using same type of suture. The innermost passes close to inner pillar of external ring. Mattress sutures may be used here. A stitch may be needed to the outer side of the cord. Note how at this point the internal oblique muscle fibers form a soft cushion for the cord, preventing constriction of latter. This row of sutures supports the second row, further tightens the canal and effects imbrication of flaps of external oblique aponeurosis. The next sketch will show how it also supports the first line of sutures, though not so directly. (Skillern.)
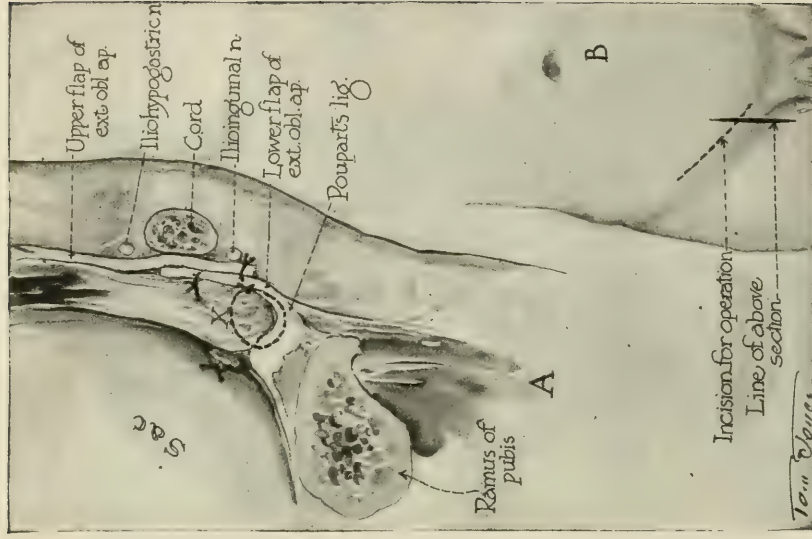
Fig. 25.—Orientation of sutured structures in sagittal section. Note stout finger-like process jammed down upon shelving ledge by first suture row; how second suture row helps hold it down in place through agency of short lower flap of external oblique aponeurosis, and how third suture row accomplishes the same purpose through agency of longer upper flap. A strong buttress against recurrence has now been established. The two nerves may be carried to the surface of the external oblique aponeurosis where internal oblique muscle contacts with outer surface of cord (see Fig. 26), thereby avoiding compression neuralgia. (Skillern.)

suturing the edges of the fibrous deep layer of the superficial fascia to each other and down upon the imbricated external oblique aponeurosis." The accompanying figures show the various steps.

To our mind, this operation in its main features, bears an exact resemblance to the original Halsted operation, except that the internal oblique muscle is not cut at the site of the internal ring. The cord is transplanted so that it lies covered only by the skin and superficial fascia, in the exact position as in the Halsted operation. The only difference is in the method of closure of the posterior wall. The first row of sutures is placed much in accordance with the method of Bassini
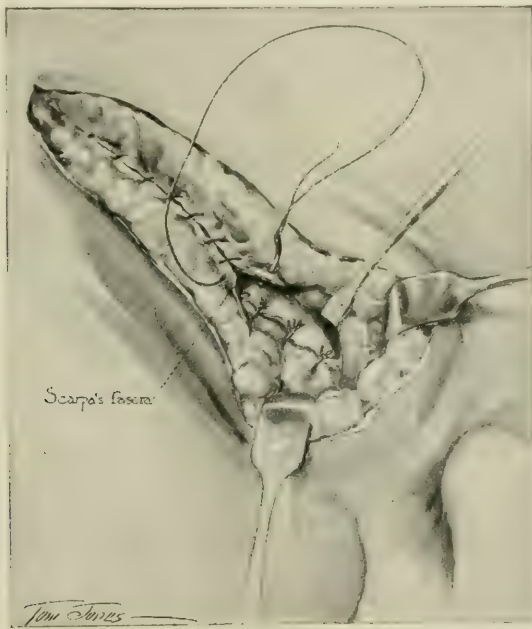
Fig. 26.—Note obliteration of dead spaces by suturing edges of deep layer of superficial fascia down upon external oblique aponeurosis. This step also approximates skin edges and after healing has occurred prevents spreading of cutaneous scar. Five or six interrupted sutures may be used instead of the continuous. The suture material is No. 1 plain catgut. (Skillern.)

or Halsted but instead of simply closing the internal oblique by approximating its edges, it is overlapped and imbricated as in the Andrews' operation. In our opinion, the one serious objection to this method is that it leaves a weak point at the site of the internal ring where the cord emerges, and the results of the original Halsted operation show that in no inconsiderable number of cases, recurrence took place at this point. Anyone who has attempted to operate on any of these recurrences, with the cord lying in this position and matted down with adhesions, knows that it is an extremely difficult operation. We can see no advantage in placing the cord in this exposed position. All of the advantages of the method, without the disadvantages and liability

of recurrence, can be obtained by overlapping the external aponeurosis over the cord instead of under it. In certain cases of direct hernia, with very weak external oblique tissue, this overlapping may be of distinct advantage.
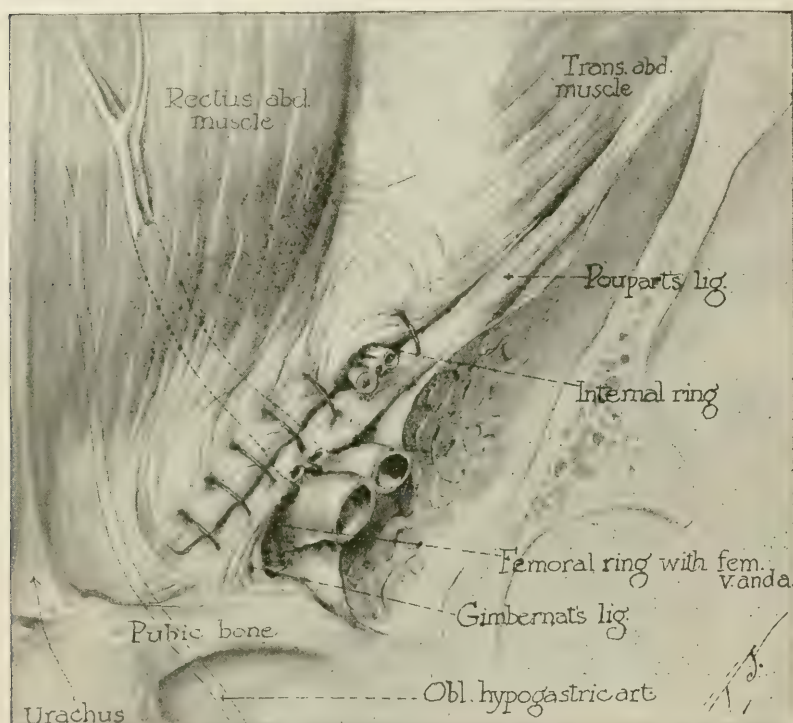
Fig. 27.—Orientation of operation field from abdominal cavity. Note great strength imparted by first suture row to that portion of abdominal wall between pubic bone and internal ring; also note lateral displacement of internal ring. (Skillern.)

Rare Types of Hernia. INTERNAL STRANGULATED HERNIA due to Meckel's diverticulum is a comparatively rare condition and one in which early diagnosis and early operative treatment are essential to recovery. A case of this kind came under the observation of the writer[1] and Stanley T. Fortuine, at the Mary McClellan Hospital, Cambridge, N. Y. The condition is so rare that in 300 cases of acute intestinal obstruction observed at the Johns Hopkins Hospital, Finney states there was not a single case of acute obstruction due to Meckel's diverticulum.

The clinical history of the writer's case may be of interest: Patient, a farmer, about thirty years of age, had always been in excellent health and had had no previous abdominal symptoms. On the day of his admission, he had had a good breakfast; shortly afterward he began

[1] Annals of Surgery, May, 1921.

to feel slight nausea and discomfort in the epigastrium. One hour later he began to have severe paroxysmal pains in the lower abdomen, which he characterized as "doubling-up" pains. These pains recurred every few minutes. The paroxysms continued to grow worse. He vomited for the first time one and a half hours after his breakfast, and twice in addition, before operation.

Physical examination showed a normal pulse and temperature; patient suffering from frequent attacks of paroxysmal abdominal pains, localized in no particular spot, centering, roughly speaking, about the umbilicus; slight tenderness in the right iliac fossa and region of McBurney's point, but no rigidity of the rectus muscle. Rectal examination negative; no mass palpable in any portion of the abdomen, no
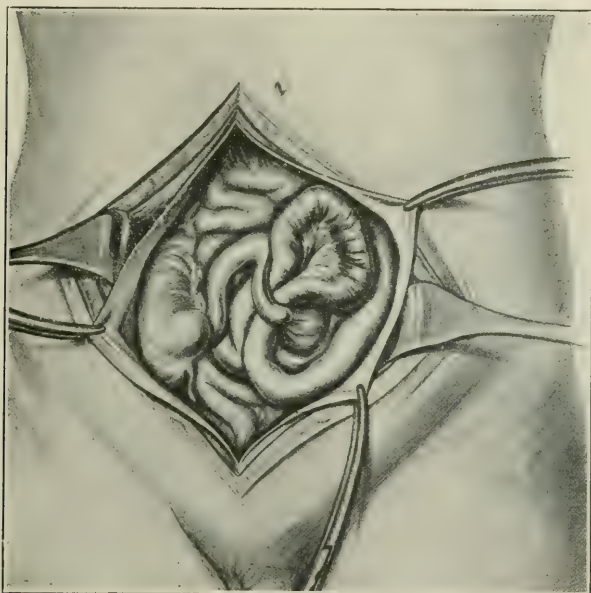
Fig. 28.—Loop of small intestine strangulated beneath a Meckel's diverticulum. (Coley and Fortuine.)

localized distention of coils of intestine in any portion of the abdomen. Heart and lungs negative. The whole aspect of the patient gave the impression of a person profoundly ill, entirely out of proportion to the physical signs of pulse and temperature,

A provisional diagnosis of acute appendicitis had been made before the patient entered the hospital.

While it was impossible to make a definite diagnosis of the condition, the severe pain and appearance of the patient—that of great shock—made us believe that immediate operation was imperative.

A normal appendix was found and finally, after careful search, a loop of small intestine about one and a half to two feet in length was found, greatly distended and dark in color, but not gangrenous, located in the bottom of the abdomen, somewhat more to the right

side than to the left, a little above the pelvis. This loop was found to be strangulated by what seemed to be another loop of intestine, firmly attached and connected with a loop of small intestine above. The constriction was so tight that it was absolutely impossible to withdraw or free the strangulated loop, which required a great deal of manipulation to dissect it off without tearing it. When the distal end was finally freed the strangulated loop slowly regained its color and, under
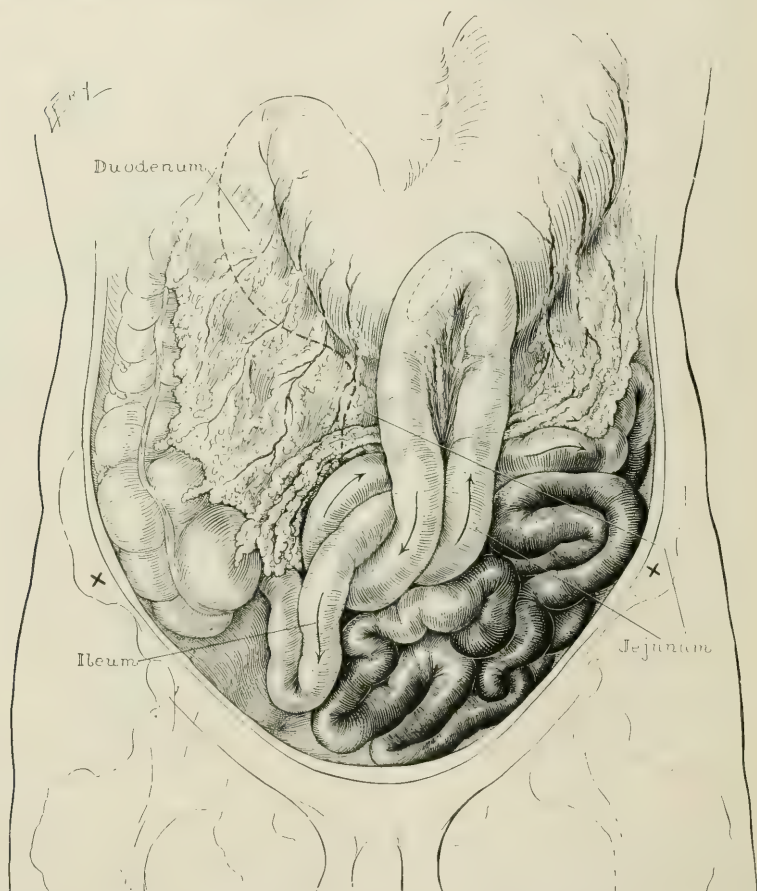
Fig. 29.—Hernia of the small intestine behind anastomotic loop of jejunum, following anterior gastrojejunostomy. (Mayo–Magoun.)

hot towels, became apparently viable. The diverticulum was clamped off close to the wall of the intestine from which it had sprung, and the opening into the intestine, which was about one and a half inches in diameter, was closed with two rows of fine chromic gut suture; the abdominal wound was closed without drainage. The patient made an uninterrupted recovery and is well at present.

The operation was performed eleven hours after the onset of the symptoms, one of the earliest cases for operation ever recorded.

Balfour, in a review of 10,000 successive operations performed at the Mayo Clinic from 1907 to 1910, reports 15 cases of Meckel's diverticulum, in only 5 of which had the diverticulum given rise to symptoms and only 1 of the 5 was operated upon for acute intestinal obstruction.
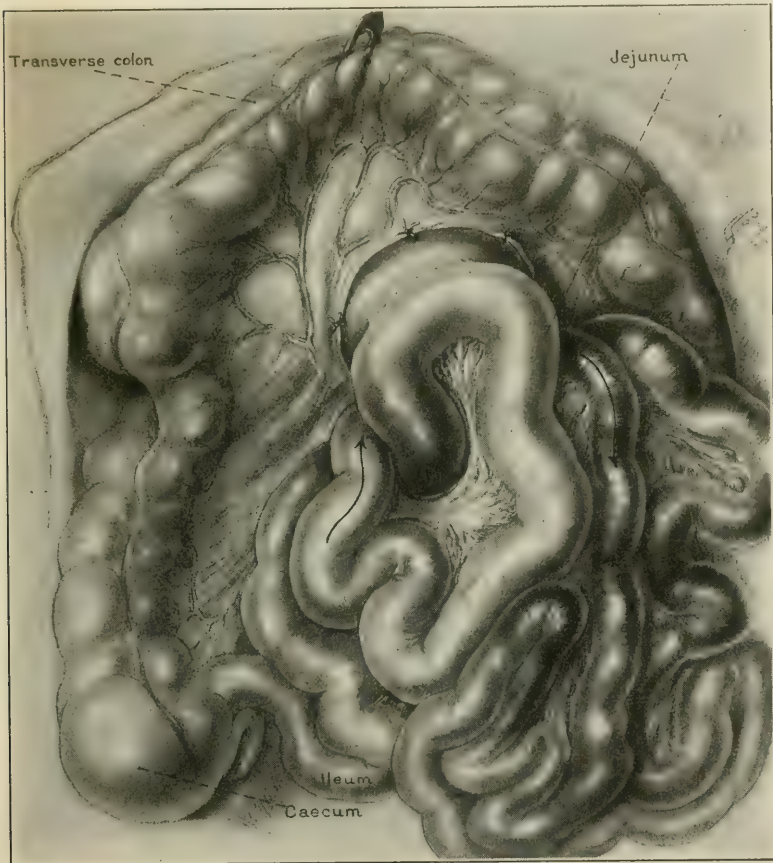
FIG. 30.—Hernia of the small intestine behind short anastomotic loop of jejunum following posterior gastrojejunostomy. (Mayo–Magoun.)

POSTOPERATIVE INTRA-ABDOMINAL HERNIA. Charles H. Mayo and J. A. H. Magoun, Jr.,[1] of Rochester, Minn., have reported 3 very interesting cases of postoperative intra-abdominal hernia. In all of these cases, the causative factor was a previous gastroenterostomy.

Moynihan, many years ago, in his monograph on Retroperitoneal Hernia, first called attention to the possibility of a hernia occurring through an abnormal aperture in the transverse mesocolon. Mayo states that, "Seven years before the retrocolic method of gastro-jejunostomy was advocated attention had been directed to the possi-

[1] Archives of Surgery, March, 1922, p. 324.

bility of the small bowel herniating through an opening in the transverse mesocolon.

"As the number of gastrojejunostomies increased, another form of internal hernia was observed. The small intestine slipped behind the loop of jejunum which is formed by every anastomosis, whether it is antecolic or retrocolic."

Moschcowitz and Wilensky, in 1915, collected 7 cases from the literature.
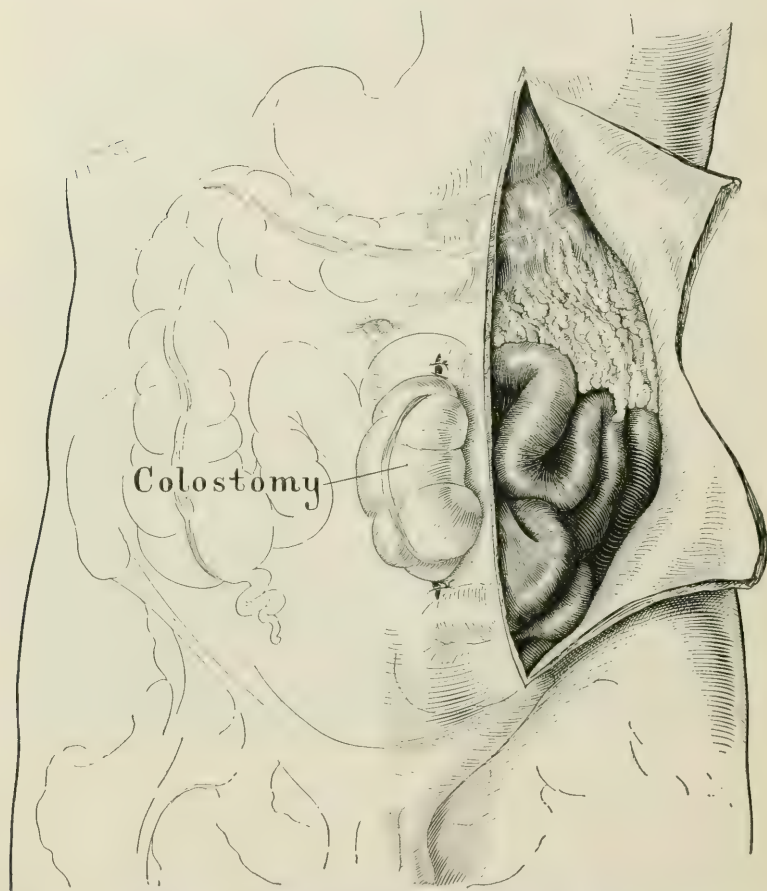
Fig. 31.—Hernia of the small intestine around colostomy. (Mayo–Magoun.)

A summary of the total number collected (10), shows that the hernia occurred in 6 cases following the posterior type of gastrojejunostomy (4 with short loops and 2 with long loops); in 2 cases following the anterior type and in 2 the type was not mentioned.

In 7 cases the hernia started on the right side and traveled toward the left. The time elapsing between the gastroenterostomy and the second operation was six days in 4 cases; eight days in 1; twelve days
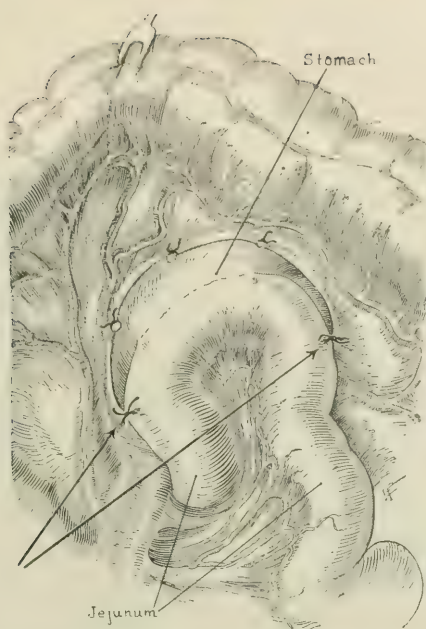
FIG. 32.—The arrows indicate the position of the sutures which would prevent the hernia shown in Fig. 2.   (Mayo–Magoun.)
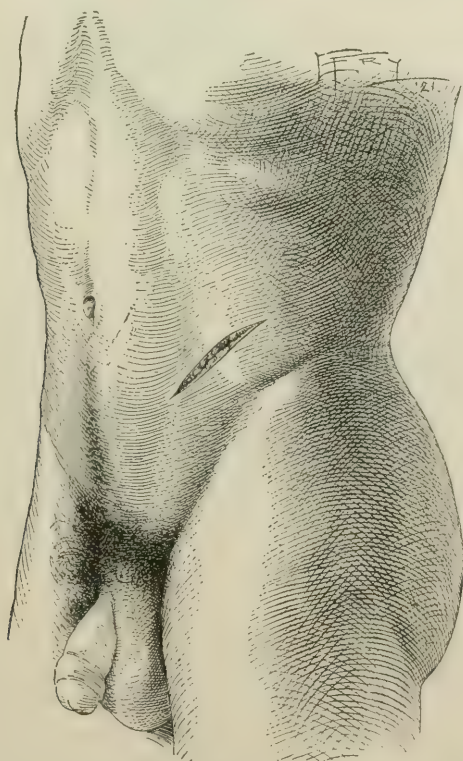
FIG. 33.—Incision for colostomy.   (Mayo–Magoun.)

in 2; fourteen days in 1 case; one year in 1, and two years in 1. Four patients died and 4 recovered.
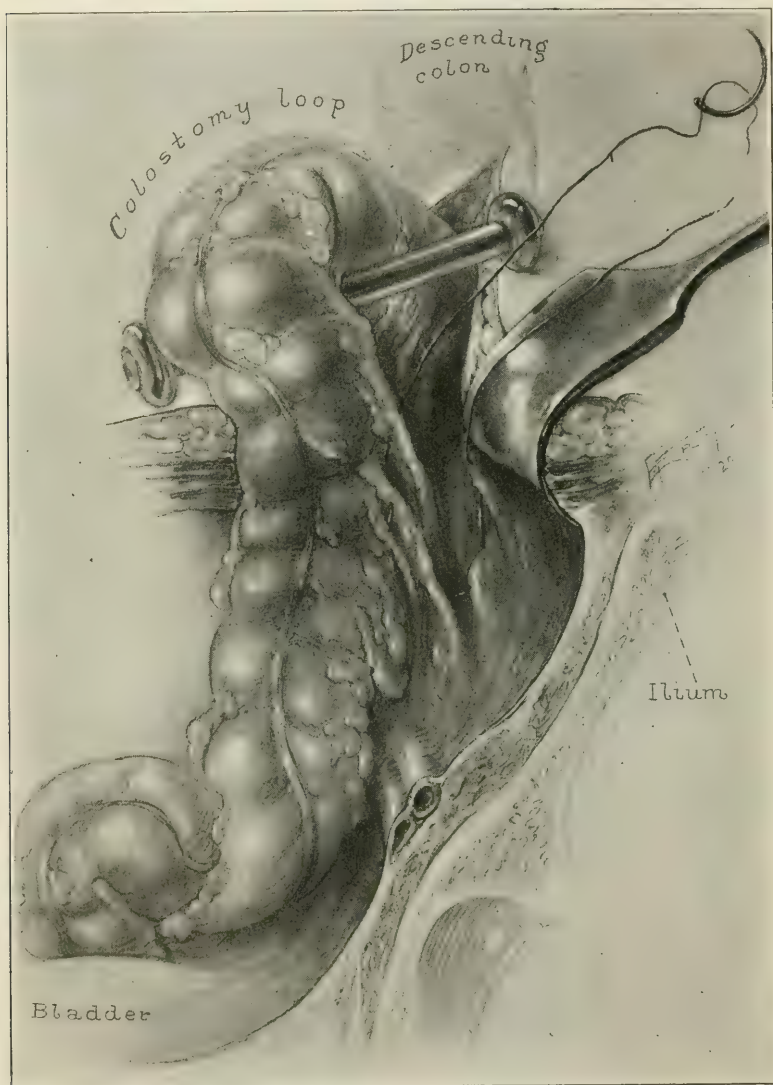
Fig. 34.—Continuous suture between parietal peritoneum and mesosigmoid, closing space on suture of colostomy. (Mayo–Magoun.)

Mayo and Magoun believe that the symptoms from this type of hernia do not appear to differ from the usual symptoms of high intestinal obstruction of acute onset, and that complication is more likely to occur in cases in which some form of chronic obstruction has distended and enlarged the loops of bowel.

The excellent illustrations accompanying their article, not only show the general characteristics of this form of hernia but also the methods of preventing its formation.
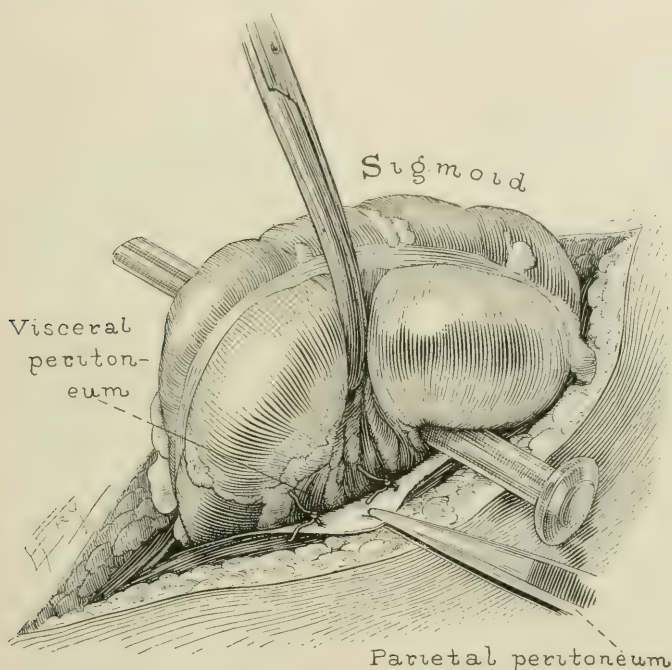
Fig. 35.—Two interrupted sutures through cut edge of parietal peritoneum and upper portion of mesosigmoid to prevent retraction of the colostomy loop. (Mayo-Magoun.)

"Traumatic" Inguinal Hernia. Moorhead[1] discusses traumatic inguinal hernia and in his conclusions brings out the fact that it is entirely erroneous to attribute the development of a hernia solely to the effect of a single act of violence. He holds that the only true traumatic herniæ are those rare cases in which the patients have had an actual penetration of the tissues of the inguinal region by a sharp object, such as, the horn of an animal or a picket fence, in which case there is apt to be severing of the muscles and fascial plane.

Moorhead classifies inguinal hernia in four degrees, *i. e.,* "*First degree hernia* means that the ring is dilated enough to admit the index-finger-tip and an impulse is present. This is designated +.

"*Second degree hernia* means that the ring is still further dilated, impulse is present," and a palpable mass appears at the ring. This is designated + +.

"*Third degree hernia* means that all the elements exist as in the second degree, and, in addition, there is a visible mass at either ring or along the canal. This is designated + + +.

[1] The Surgical Clinics of North America, December, 1921.

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"*Fourth degree hernia* means that the mass enters the scrotum.   This is designated + + + +."

He takes up the question of "traumatic hernia," under three phases:

"1. Is there any such thing as 'traumatic hernia,' one arising solely from a single act of violence?

"2. If not, how does a single act of violence affect the development of hernia?

"3. And again, what is the effect of repeated acts of violence in the production of a hernia?"

He draws attention to the inguinal canal and the uterine cervical canal, pointing out that each has an internal and an external opening with a normally fixed caliber which is adequate to the physiologic demands of each.   By the continued stress of intra-abdominal pressure, both of these canals dilate, the one eventually giving birth to a fetus, the other, to a coil of intestine or omentum.   As in the case of slow progressive dilatation of the uterine canal, due to repeated or inter-mittent intra-abdominal pressure, so it is in the case of the inguinal canal, the result of long-continued pressure and not the result of any sudden abdominal contraction.   In his words, "A single intra-abdominal contraction never causes a dilatation of the cervical canal or of the inguinal canal; the process in both cases is slow, the product of a con-tinuing, oft-repeated force."   Therefore, in answering question No. 1, he says, that, a single act of violence cannot cause a hernia unless the violence has caused a severing of the overlying muscular and fascial protectives.

In answering question No. 2, *i. e.*, what is the effect of a single act of violence in the development of a hernia, he brings out the importance of what he calls the ptotic type.   An individual with ptosis has all the predisposing factors which tend to make a hernia possible.   In the first place, his muscles are lax; the internal and external rings are open, probably being dilated by varicosities—to which Moorhead draws the analogy of Barnes' bag in the cervix.   Such an individual has probably had a first degree hernia for years and was probably born with a patent inguinal ring.   In such an individual, one final act of violence associated with excessive intra-abdominal pressure, may cause the hernia to make an appearance, which, however, has been in a potential state for years. As he well points out, if a hernia was actually caused by a single act of violence, the trauma attendant upon it would make itself felt by the production of pain, tenderness, nausea, and probably some discoloration of the parts, it being absurd to believe that a piece of intestine or omen-tum could be forcibly crowded into a normal ring or canal without the knowledge of the patient, until hours, days, or weeks later, which is the usual history of the great majority of cases.

As to question No. 3, *i. e.*, what is the effect of repeated acts of vio-lence in the production of a hernia, Moorhead again attributes its effect largely to the individual physique and to the type of violence, showing that men accustomed to lifting heavy weights, athletes and others who are accustomed to throwing excessive strain on their intra-abdominal muscles, as a rule, are not subject to hernia, owing to their

symmetrical muscular development. He points out that, workmen who use their muscles as do athletes, are not apt to develop hernia whereas men whose occupation tends to develop one set of muscles without commensurate development of others, show a high instance of hernia.

There is no question that repeated or intermittent intra-abdominal strain of an excessive character, is quite capable of enhancing a hernia once formed, although, there is an inherent tendency of every hernia to increase in size regardless of the activities of the individual.

Among some of the observations which Moorhead brings out may be mentioned the large proportion of adults with hernia who are unaware of their condition. In proof of this, he cites the large number of individuals whose hernia was discovered at the time of their physical examination for extrance in the recent war. He shows that, with a swelling fully developed on one side and a partially developed one on the opposite side, the etiologic factor is much more apt to be an anatomic defect than a traumatic one. The family history of hernia is mentioned, showing the fact that it seems to be due to a transmitted strain of muscular defect and we have noticed very frequently in our experience, that a ruptured individual gives a history of the same condition in other members of the family.

Moorhead closes with a description of the modified Bassini technic which does not differ in any essential particular from that of the method usually described. However, it seems worth while to include his comments on the factors necessary to obtain a successful cure. They are:

"1. Ability to obtain a high tie-off and narrowing of the neck of the sac. If this is attained, the preëxisting diverticulum of the peritoneum is definitely abolished.

"2. Ability to firmly coapt muscle (internal oblique and conjoined) to the shelving edge. If this is attained, an effective barrier is built up against further intra-abdominal strain and subsequent direct hernia.

"3. Ability to lengthen the distance between the rings by transplantation of the cord. If this is attained, any hernia seeking escape at the rings will find the exits blocked by a layer of muscle and fascia instead of by tissues far less resistant.

"4. Ability to obtain primary union. If this is attained, all newly joined barriers offer lasting stability."

As regards recurrence, Moorhead points out that the rate in direct hernia is approximately double that of the oblique and its instance is much higher in individuals over forty-five years of age than in those under that age. Furthermore, in working people, the rate is greater than that in the non-working class. He gives his own rate of recurrence in working males as between 5 to 10 per cent.

Recurrent Hernia. A subject that has always been of interest to surgeons is that of recurrence following attempted cure of inguinal hernia by operation. Thus Sheen's [1] contribution to this phase of the subject is well worth consideration. He makes a number of interesting

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[1] Lancet, April 9, 1921.

observations which are based on the conditions found at the time of reoperation. For instance, his experience shows that the recurrences are almost invariably small where the original hernia was small. The factor of infection was found in only 1 instance in his series, hence, recurrence could not be attributed to weakness at the site of previous operation. The most important point he noted, however, is the fact, that "The region of the neck has remained apparently virgin ground." His findings with relation to the position of the cord have forced the conclusions upon the reviewer that, in most cases the repair had been effected without transplantation of the cord, a method which, by means of parallel series of cases operated upon at the Hospital for Ruptured and Crippled, we have shown to be followed by a higher incidence of recurrence than where transplantation was done. There was no direct evidence of ligation of the sac other than scarring either inside or outside of the sac itself. This, it would seem, is to be expected. The difficulty and tediousness of the secondary operation is mentioned and anyone who has had occasion to do many reoperations is familiar with this fact.

The conclusions arrived at by Sheen as to the etiology of recurrences are as follows: Primarily, the cause seems to be failure to remove the deeper part of the sac. This we firmly believe is of the utmost importance and in many cases of small, indirect hernia, it may be only necessary to secure a high ligation of the sac to obtain a complete cure. As an occasional cause may be the failure to find a small sac, or the subsequent development of a direct sac where the original operation was for an indirect hernia. It may be here interpolated that if in every operation for hernia, after the sac has been opened, the operator insert his finger into the sac and palpate mesially the region of Hesselbach's triangle (the site of direct hernia) the quality and thickness of this portion of the abdominal wall can be ascertained and if there be a bulging in this situation the peritoneal lining (*i. e.*, potential sac) can be peeled externally by traction on the sac with the finger still in place and gauze wiping will convert the potential double or saddle-bag sac into one entirely indirect, the deep epigastric vessels being guarded during the blunt, gauze dissection. For further description of this valuable step in the management of hernia operations the reader is referred to the article by Downes who brought it to the attention of the profession and to Sheen's article which refers to palpation for possible direct hernia. The majority of the remaining recurrences are of direct herniæ.

To lessen the frequency of recurrences, Sheen, wisely suggests that hernia operations should be performed only by those who are thoroughly trained by actual operative experience, pointing out that "a well-performed operation demands a high degree of technical knowledge and skill." He cautions also overlooking a direct sac in cases where the obvious rupture is indirect in type.

As regards operative technic, Sheen takes issue with the Bassini operation as ordinarily performed and states that he prefers in most cases, especially where the hernia is direct or where the sac is not unduly

large, to leave the cord in its normal anatomic relationship and not transplant it. This is not in accordance with the views of most American surgeons of large experience. He advocates "Division of the internal oblique in the line of the canal outward for about an inch" especially in adults, for the reason that it enables one to secure better exposure for performing high ligation of the sac.

We feel that a small blunt retractor can be utilized to give ample exposure in this situation and thus avoid cutting an important part of the tissues upon which we rely for our repair. We, moreover, are not in favor of the use of wire filigree in the repair of any type of hernia a step to which Sheen states, he sometimes has recourse, as in our experience, the use of such a foreign body tends to produce subsequent irritation and pressure atrophy of the adjacent tissues, and sinus formation may supervene.

Sawyer, in *Surgery, Gynecology* and *Obstetrics*, July, 1921, page 38, describes a condition which is commonly known as *Richter's hernia*, although, his title is "Acute Partial Enterocele" which is, perhaps, more anatomically definitive.

A partial enterocele is an abdominal hernia in which only a portion of the circumference of the gut protrudes through a hernial orifice as a diverticulum. Obviously, this does not, as a rule, completely obliterate the intestinal lumen but reduces its bore.

The first comprehensive study of this condition was made by Treves in 1887, almost a century after Richter's first real scientific description of the condition which now bears his name. Treves was able to collect 50 cases and stated that he considered the condition rare but not a curiosity.

Statistics show that it occurs more frequently in woman than in men and in adults than in children. Its most frequent site is a femoral hernia. The theories of the causation of this condition are ingenious and varied but not as yet satisfactorily proved. The action of intra-abdominal pressure on a loop of intestine which may have become adherent over a hernial orifice, associated with pressure within the bowel, is believed to be a factor in some cases. Stahl offers the theory that the condition may be due to irregular action of the muscles in the gut wall, or as he calls it "disordered peristalsis."

Although any portion of the bowel may be involved in this form of hernia, the ileum is the most frequent site. That portion of the gut which is farthest from the mesenteric attachment is most frequently involved and the line of constriction is circular. The obstruction to the fecal current is naturally variable and therein lies the diversity of symptoms, *e. g.*, constriction may obstruct the passage of feces but still permit the gas to escape. In one-third of the cases, Sawyer found symptoms of a typical strangulated hernia, while in the remainder the symptoms were less severe and oftentimes misleading. The pain may be sudden and sharp, located in the region of the hernia, but it is often diffuse over the abdomen without localization. Where there is no localized pain at the hernial site, and with the "colicky" pain referred to the epigastrium, appendicitis is simulated. The vomiting is less

frequent and severe than in ordinary complete obstruction, but it usually occurs. In only a small percentage of cases does actual fecal vomiting take place. As regards the action of the bowels, any degree from a diarrhea to complete stasis may occur. In the majority of cases there are bowel movements after strangulation has taken place. On the other hand, meteorism is uncommon because of the escape of the gas through the only partially obliterated lumen which tends to prevent abdominal distention. When the hernial protrusion is small, it may pass entirely unrecognized. In 50 per cent of Treves' series, it was never recognized during life. The blood count is of little importance and the temperature, pulse, and other vital signs, are as in other strangulations.

The treatment is immediate operation and in most cases attempts at reduction are not justifiable. The type of operation depends upon the condition of the bowel, which may be in any degree, from a mild congestion to a gangrene with perforation. Where the protrusion is small, the bud of gut may be invaginated somewhat in the manner of an appendix stump, the purse-string suture not vitally interfering with the lumen of the gut. This is particularly valuable where the patient's condition hardly warrants a resection.

The prognosis, as revealed by the cases in the literature, is extremely disappointing since it shows a mortality of over 50 per cent of the cases operated upon. This is, no doubt, largely due to the late diagnosis and to the fact that gangrene occurred more promptly than in the ordinary strangulated hernia because the constriction was applied to the gut without the cushioning protection of the constricted mesentery.

The writer has operated upon 3 patients for Richter's hernia all of whom recovered. The last patient operated upon (February 8, 1922) was a woman, aged fifty years, and the hernia femoræ had been strangulated for forty-eight hours, the condition not having been recognized. The overlying sac was greatly inflamed and one-eighth of an inch thick. The loop of ileum, more than half the lumen of which was very tightly constricted, was a of very dark color but not necrotic. It was very difficult to relieve the constriction without injuring the gut.

The patient made an uneventful recovery.

Sliding Hernia of the Ureter. The extreme rarity of this condition as evidenced by the paucity of references in the literature may be explained partly because of its absolute infrequency and also on account of the ease with which the condition can be overlooked.

Ross and Taylor[1] find only 1 case reported previously, and that very recently, by Griep.[2] So unusual were the conditions in their case that we feel it desirable to copy from the protocol of the case:

F. O., a Polish coal miner, aged thirty-three years, was admitted to the University Hospital, Philadelphia, on October 10, 1920. For the past eighteen years he had had a right inguinal hernia which had

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[1] Annals of Surgery, May, 1921.
[2] Med. Klin., June, 1920, **16**, 24.

grown so large as to cause some disability but no discomfort or pain. The previous history was negative save for smallpox in childhood.
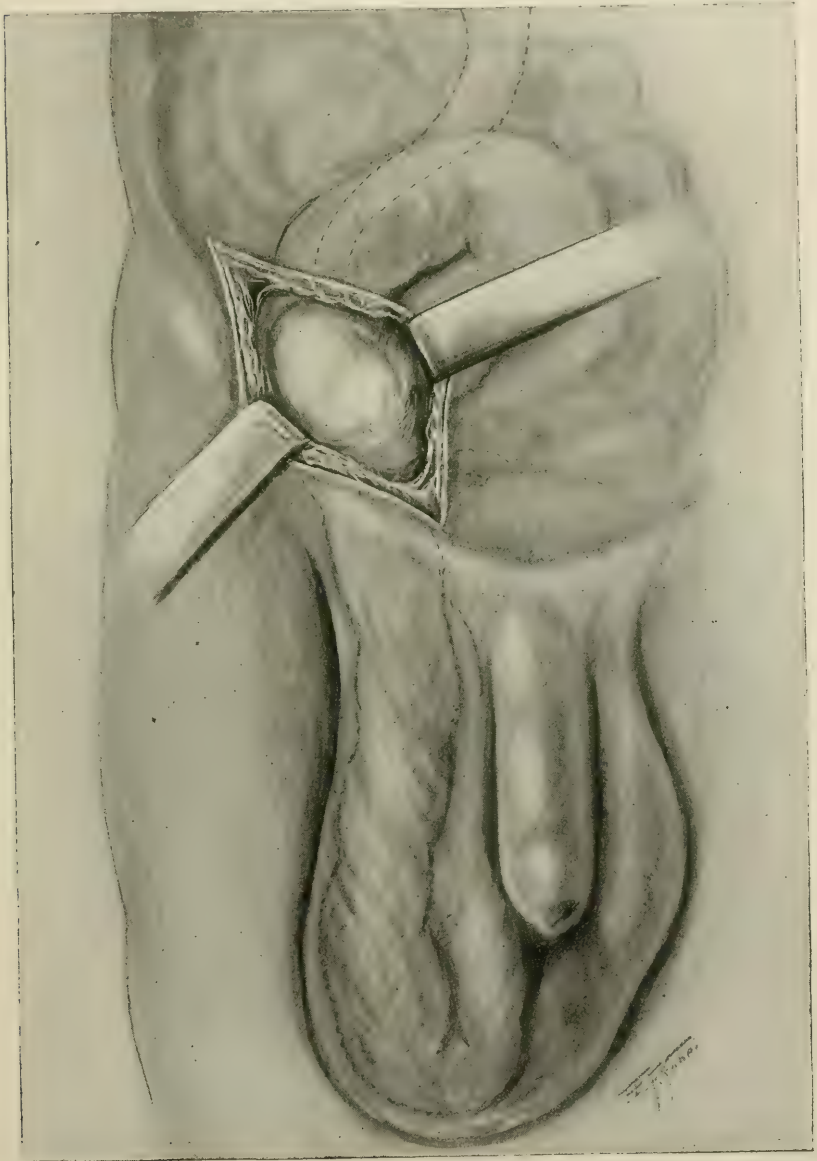
FIG. 36.—Hernial sac exposed.. (Ross and Taylor.)

The patient complained of nothing but the hernia. After the operation it was determined with the aid of an interpreter that for the preceding two years the patient had some frequency of urination during the day,

voiding about every two hours.   There was no two-stage micturition
occasionally met with in hernia of the bladder.
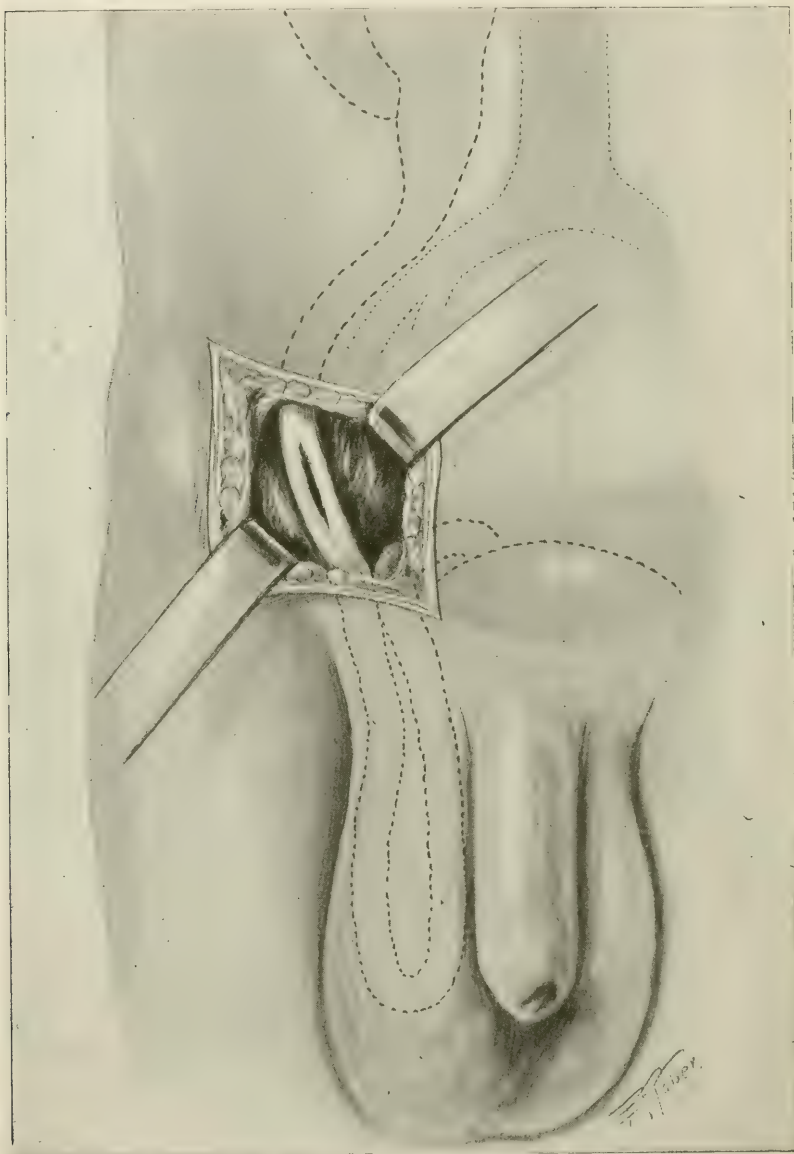
FIG. 37.—Sac and contents removed.   Ureter in position.   (Ross and Taylor.)

Physically the patient presented no abnormalities save indistinct
pock-marks about the face and neck, and a very large right scrotal
inguinal hernia. When the patient stood, the scrotum reached half
way to the knee, and its dimensions were about those of a football.

Testis

Mesonephros
(Wolffian body)

Mesentery
of gland.

Genito-inguinal lig.

Kidney

Testis

Lig. of the testis
Genito-inguinal lig.

Bladder

Mesonephros
(later Epidid.)

Mesonephric duct
(later Vas. def.)

To abdominal wall

Kidney

Bladder

Testicle

Gubernaculum
testis
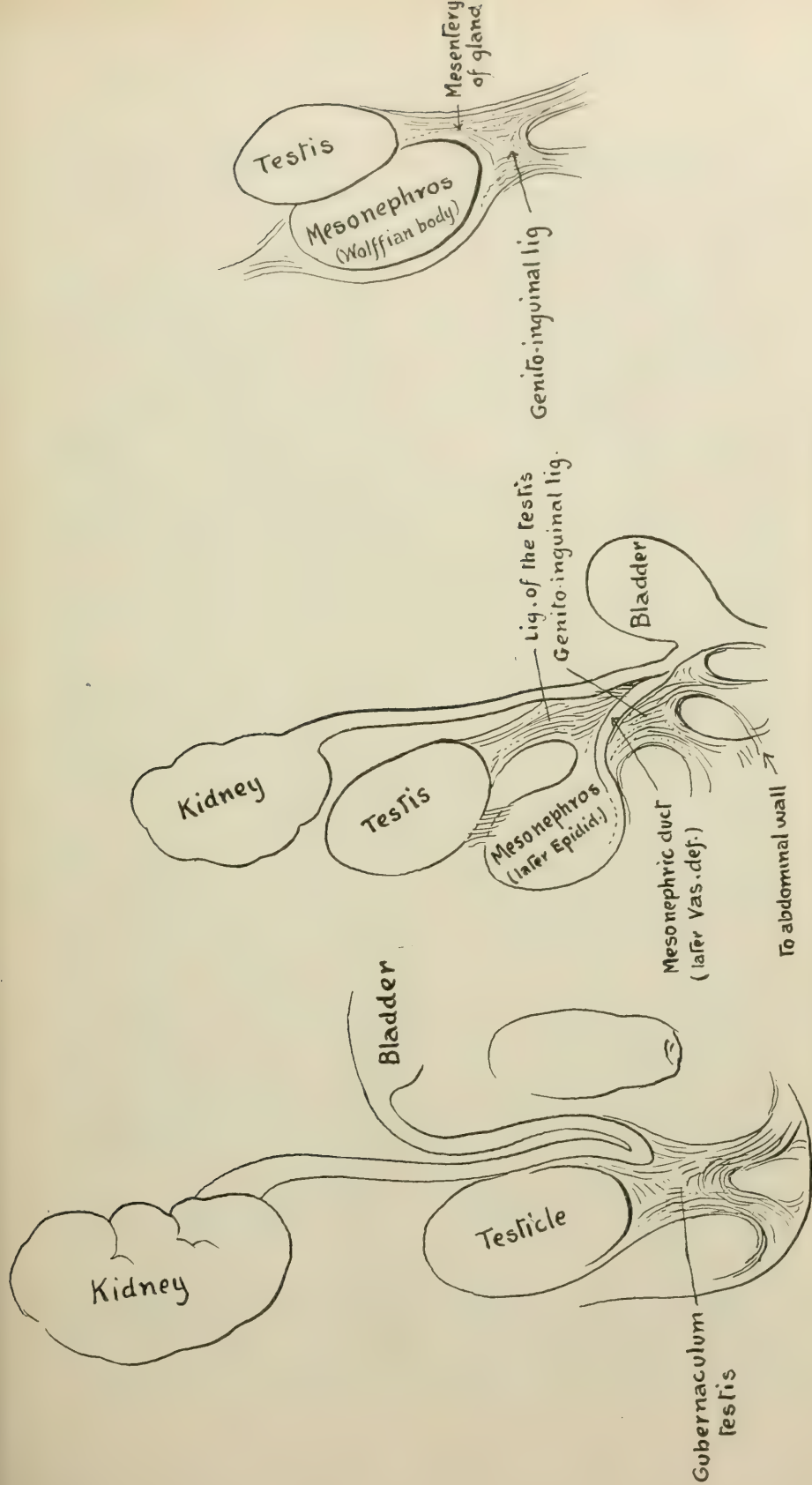
Fig. 38.—Embryonic development of prolapsed ureter. (Ross and Taylor.)

The hernia was easily reducible through an enormously dilated inguinal canal. The testicle occupied the most dependent portion of the scrotum, and the contents of the sac yielded a resonant note throughout.

Blood-pressure, 14L-85; the blood-count normal; phthalein elimination, 45 per cent in two hours and ten minutes.

Operation (October 11, 1920). Dr. George G. Ross exposed the sac in the usual manner and freed it without difficulty from its attachment to the bottom of the scrotum. The sac was about seven inches long, three inches in diameter and one-eighth of an inch in thickness.

The sac was opened, and its contents, composed entirely of small intestine, reduced without difficulty. The sac was then separated from surrounding structures in the neighborhood of the internal ring. A protrusion about the size of a golf ball was noted immediately to the outer side of the neck of the sac. It was thought to be a part of the sac or a second sac, since it had the same tough, thick appearance, and was accordingly incised. Urine of ammoniacal odor immediately welled out. Thinking that a very large diverticulum of the bladder had been opened (although it lay to the outer side of the sac) a sound was passed per urethra into the bladder. The finger in the supposed diverticulum was unable to palpate the sound in the bladder. Dissection proceeded, and it became evident that the ureter was dealt with. It descended to the depths of the scrotum in a single loop and returned to its insertion in the bladder, which was not implicated. About ten inches of extra-abdominal ureter was thus dissected with difficulty from the peritoneum forming the posterior wall of the sac, to which it cleaved tenaciously. The ureter was about one inch in diameter and its wall was about one-eighth of an inch thick.

Since the ureter had been jeopardized by this dissection it was deemed necessary to remove the kidney, and this was speedily done by continuing the inguinal incision upward into the right loin. The pelvis of the kidney was distended to about three times its normal size, and the kidney itself was displaced downward about one and a half inches and appeared hard and atrophic. The entire ureter was removed with the kidney, its lower end being tied near the bladder. The muscles and fasciæ were closed in layers, a cigarette drain provided for the loin, and an indwelling catheter for the bladder. Hypodermoclysis caused a prompt rally from a moderate shock. Convalescence was marked by a severe bronchitis, an orchitis, cystitis, and limited infection of the wound. The latter cleared under Dakin's treatment, while the bladder condition improved with mercurochrome instillations. There was no urethral or prostatic obstruction.

Six weeks after operation patient was discharged with a phthalein output of 40 per cent, no evidence of recurrence of hernia, and in good general condition. Unfortunately, the patient refused cystoscopic examination.

In discussion of the case, the authors endeavor to explain the interesting question as to why the ureter alone slid, and the cecum, ascending colon and other organs failed to do so. "If," they say, "a hernia of such size was able to pull down the ureter, according to the

theory of Moschcowitz, why should it not have pulled down other adjacent extraperitoneal organs?" Their explanation, which seems reasonable, is based on the assumption of a congenital anomaly due to the failure of early differentiation of the Wolffian duct which forms the attachment between the genito-inguinal ligament (by means of which the testis descends into the scrotum) and the ligament of the testis. The ureter, which develops as a stalk from the Wolffian duct during the fourth week of fetal life, lies anteriorly and to the outer side of the Wolffian duct. It is therefore in a position where it could be dragged down at the time of the descent of the testis, should it adhere to these two guiding ligaments, or should differentiation fail to occur early enough.

It is to be hoped that with the report of this, the second case of sliding hernia of the ureter, surgeons dealing with large sliding hernias will be on the lookout for other similar cases.

Pudendal Hernia. James F. Grattan's[1] case is of great importance as in addition to the rarity of the condition, as shown by the small number (11) of cases collected by Moschcowitz[2] it is the only one of which we are aware which may properly be classed as an operative cure.

The difficulty in making a diagnosis, the frequency with which the condition is confused with prolapse of the rectal or bladder wall (rectocele or cystocele) and the close similarity of symptomatology to the latter conditions are all brought out in Grattan's communication. Moreover, he explains the anatomic situation of the defect in the pelvic floor as being that triangular area, normally weak, bounded laterally by the ischiocavernosus muscle, medially by the constrictor cunei and posteriorly by the transversus perinei. His case differed in one important respect from those reported by Moschcowitz, namely, that instead of the hernia presenting in the vulva it was most prominent in the adductor region of the thigh. In this case he believes the hernia to be due to a tear in the levator ani muscle consequent on a difficult labor (twins).

His operative procedure is worthy of some consideration. It seems to us that his choice of the abdominal rather than external approach was a most happy one. First it gave excellent opportunity to make out the landmarks and to preserve without risk of injuring the contents of the sac (in his case, sigmoid) and secondly, it enabled him to carefully close the actual rent in the muscles (or neck of the sac) in a far better and more satisfactory manner than is conceivable through an approach from below. The fact that this is the only known cured case is substantiation enough, we believe, of the superiority of the upper approach.

We quote from his description of the operation:

"A suprapubic incision extending from the symphysis to the umbilicus was necessary on account of the extremely fat abdominal wall. The exposure of the pelvis was difficult because of the great amount

[1] Surgery, Gynecology and Obstetrics, February, 1921.
[2] Reported in the American Journal of the Medical Sciences, 1918, **156**, 394.

of intra-abdominal fat and the risk of the exaggerated Trendelenburg position in an adipose subject. Exposure of the pelvic organs finally revealed descent of the sigmoid loop through a triangular opening in the floor of the pelvis. This opening was bounded anteriorly by the posterior reflection of the left broad ligament, mesially by the lower segment of the uterus and the left utero-sacral ligament, laterally and posteriorly by the rectum. The sigmoid being fixed at its point of continuation into the rectum, appeared to slide down along the posterior surface of the broad ligament and disappear through the hernial opening. Practically the entire loop was out of view. Much to my surprise gentle traction brought the entire sigmoid loop out of the sac. There were no surface adhesions and no evidences of constriction at any point. The opening was triangular in outline with the utero-sacral ligament forming the base, the reflection of the broad ligament the anterior arm and the rectum the posterior arm of the triangle. I inserted my left index and middle fingers downward into the sac and had the nurse uncover the inner side of the left thigh and identify the fingers through the skin covering the sac. There was no process of the sac descending into the left labium as in the cases of "pudendal" hernia reviewed by Moschcowitz. However, the exit and course of the descent in this case was undoubtedly the same, the final destination being the subcutaneous tissue of the upper adductor region of the thigh rather than the labium.

Needless to say, no attempt was made at extirpation of the sac. Its depth, the adipose status of the patient, her age, as an argument against prolonging the anesthesia needlessly, precluded this. With great effort and difficulty I passed five or six mattress sutures of double Pagenstecher linen across the long arms of the triangle and succeeded in closing it tightly and completely. To make doubly sure, I whipped a continuous suture over the line of mattress sutures, taking another reef in the broad ligament. This last step caused a version of the uterus backward and to the left superimposing the fundus over the site of the hernial opening. The sigmoid was anchored to the left psoas muscle at the brim of the pelvis and again about two inches above that point, the idea being to prevent its descending to its habitual location in the vicinity of the hernial opening.

The abdomen was closed by layer sutures. The patient made an uneventful recovery. She was kept in bed for three weeks. Mineral oil was used for six months following the operation to assure a daily evacuation. This is not necessary at present. The sense of prolapse and the rectal irritation of which the patient previously complained, have never been experienced since she left the hospital."

Van Zwalenburg[1] who, in March, 1911, operated upon an old lady for the radical cure of double obturator hernia, has published the final notes on the case, which, summed up, are as follows:

"This patient was a woman, aged seventy-six years, very much emaciated, with a history of recurring attacks of abdominal pain going

[1] Surgery, Gynecology and Obstetrics, October, 1921, p. 429.

back for twenty-six years. A diagnosis of double obturator hernia was made and an operation for radical cure performed. The abdomen was opened; a pair of forceps was introduced into each sac; the sac was inverted and stitched over and over with chromic catgut suture. The whole was quilted down upon the obturator foramen imitating a method used by C. H. Mayo in femoral hernia.

FIG. 39 (above).—Hernial sac in obturator hernia.
FIG. 40.—Incarcerated ileum.   (Zwalenburg.)

"The old lady made an uneventful recovery and was thoroughly relieved from colic-like pain for six or seven years. At the end of this time some of the former pain gradually recurred; although of a much less severe or continuing character. Her emaciation continued and if anything increased, although she was otherwise in very comfortable health.

"During August, 1920, she was vacationing at the beach and was taken with pain about the 17th, which continued with varying intensity without the usual complete remission which had obtained on previous occasions. On August 27, she was put in an ambulance and brought to Riverside, a distance of sixty miles. She was not seen by a physician during all these ten days. When I saw her that evening soon after her arrival, she was vomiting frequently, in fact was

losing more fluid by emesis than she could take in. She suffered the usual thirst present under such conditions. Her abdomen was considerably distended, but was only moderately tender and practically confined to the right lower quadrant. Through the vagina I could make out a fold of tissue leading to the obturator foremen but I could not dislodge it. I presumed this was the intestine entering this hernial sac. This assumption later proved to have been correct.

"I made the diagnosis of strangulated obturator hernia. On account of her age, now eighty-five, the ten days which had elapsed since the incarceration began and her profound prostration, operation was only tentatively considered and forcefully rejected by the family. She died the next day and came to autopsy the day following.

"At autopsy we found the abdomen fairly distended. Opening the abdomen we found the small intestine dilated and the ileum leading down to the right obturator foramen where a loop about three feet from the cecum was fairly incarcerated in the hernial sac. It was impossible to draw the intestine back into the abdomen, and, not until the right sac had been dissected out and the constriction relieved, could the loop be liberated from the opening. To our surprise there was no strangulation present. The bowel was simply incarcerated, completely preventing the alimentary contents from passing this point. Complete obstruction without strangulation.

"The cause of death was doubtless the toxemia which accompanies intestinal obstruction."

Lewisohn[1] makes a plea for thorough exploration of the intra-abdominal organs in cases operated upon for epigastric hernia. He says that it is only during the past ten years that attention has been adequately called to the fact that simple operation for epigastric hernia resulted in relief from gastric symptoms in only a certain and not too large a percentage of cases.

Capelle, reporting from Garrè's clinic, states there were 31 patients operated upon previously (six months to eight years) for epigastric hernia; 4 died from cancer of the stomach within two years of the original operation; 6 had recurrences of their hernia, and 12 had recurrences of their gastric symptoms; only 9 (29 per cent) were entirely cured.

Schloffer reaches the same conclusion, and reports 2 cases previously operated upon elsewhere for epigastric hernia, in whom the symptoms persisted and reoperation was performed. He found a carcinoma of the stomach in 1 case and carcinoma of the splenic flexure in another, the previous operators having erroneously ascribed the gastric symptoms to the presence of an epigastric hernia.

Ertrand collected 15 cases from the literature of the coexistence of epigastric hernia with ulcer or cancer of the stomach.

The three organs, which are most frequently found to be the cause of the symptoms mistakenly described as "epigastric hernia," are the stomach and duodenum, the gall-bladder, and the appendix. In the 13 cases reported by Lewisohn, 11 had lesions in the stomach or

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[1] Surgery, Gynecology and Obstetrics, June, 1921, p. 546.

duodenum; therefore he makes the earnest plea for a thorough roentgen-ray examination of the gastro-intestinal tract before operating upon epigastric hernia. In fact, he states the roentgen-ray examination of the gastro-intestinal tract should be part of the routine examination in all cases of epigastric hernia.

As we realize the inability of the roentgen ray to demonstrate the great majority of gall stones we are forced to reach the diagnosis of gall-bladder disease in coexisting cases of epigastric hernia largely on the character of the attacks, the history and the general physical examination; therefore, Lewisohn's main plea is for an adequate incision to enable a thorough exploration of the abdomen.

In the past year we have seen at the Hospital for Ruptured and Crippled, an interesting case which bears out Lewisohn's contention. A patient with a moderate-size epigastric hernia presented himself for examination. He was complaining of marked inability to take solid food (although milk and eggs seemed to agree better). His hernia was so definite that at first we considered his symptoms to be referable to it but decided, before recommending him for admission and operation, to give him a few swallows of barium paste and have a roentgen-ray picture of his esophagus and stomach. This was done and revealed a typical constriction of the esophagus over a distance of 4 to 5 cm. and undoubtedly represented an esophageal carcinoma. He was then referred to a surgeon for an esophagoscopy and has been treated with considerable relief by radium since that time. It is evident that this case could have easily slipped by and been operated upon without the slightest relief to his symptoms. We are more and more coming to realize the danger of ascribing the patient's symptoms to some pathologic condition which is self-evident and are appreciating the fact that the presence of one condition does not, in any sense, rule out coexistent disease elsewhere.

SURGERY OF THE ABDOMEN, EXCLUSIVE OF HERNIA.

By ABRAHAM O. WILENSKY, M.D.

EVERY branch of human endeavor—science, industry, social organization—has undergone momentous changes in our times, but in no branch have the alterations been more marked than in medical and surgical knowledge and practise. America has been quick to assimilate the best that the European countries have had to offer and has, in turn, taken the initiative in the pursuit of knowledge and in the fruitful application of that knowledge to practical uses.[1]

Owing to the great extent of clinical medicine and surgery there has gradually developed a variety of medical and surgical specialities. Because of this, group medicine, in some form becomes the only means by which the patient can receive the attention to which these advancements of medical science entitled him. Properly considered, this is no financial arrangement, except for minor details, but a scientific coöperation for the care of the sick. The value of such coöperation, especially in obscure abdominal cases, is now well recognized; and this group method promises to give the benefits of specialization without any of its disadvantages provided proper correlation is practised.[6]

Group medicine has one very outstanding advantage. It takes away the liabilities of any one personality and substitutes therefore the average capabilities of a number of men. The chances of error are minimized thereby in direct proportion to the number of minds gathered in the group; the vagaries of the brilliant intellect are checked up in the steadiness of the slower-working thinker; and the whole, as far as it is humbly possible, reduces the medical observation of any patient to the accuracies of a machine.

So it is in practical surgery. Human welfare is measured by the greatest good to the greatest number. It is to humanity's advantage that instead of having a limited number of exceptional technicians—very limited for many reasons as far as the average run of peoples go—that there be a sufficient number of average, trustworthy workers. The results of surgery are not the results of any one person; rather, are they the combined results of every one working in the field. Group medicine will be a powerful developer of this idea and humanity will be benefited thereby in that groups can be scattered broadcast throughout the country; at present, these are limited to the major centers of social and medical life.

The educational value of information obtained by a study of *end-results* has long been impressed on all medical men. It was not long before surprising factors became apparent which led to the substitution

of definite data for vague impressions. It was a shock to learn that there are poor or bad results of which there had been previously a blissful ignorance. Such experiences have made Gibson[5] and his co-workers feel a certain reluctance about accepting statements on such matters unless there is evidence that a systematic effort is made to check up all results.

Much may be learned by a study of a large mass of surgical material. W. J. Mayo[6] points out that such an investigation will sometimes point out a way by which an intensive study of outstanding failures may be made to yield valuable suggestions. Statistics indicate that some deaths and many poor results are apparently due to accidental or preventable causes and occur with a regularity so definite that their incidence can be foretold from year to year. "That which can be foreseen can be prevented." It is difficult to secure comparable results from different hospitals. For instance, in some hospitals a patient with an inoperable condition remains in the hospital until death in which case the operation is charged with a death; or the patient, having gone home within a few days of the exploratory operation, the record of the hospital does not indicate that a death had occurred. Similar causes for other similar grotesque or ambiguous statistics are common knowledge. What one needs for accurate knowledge is the picture obtained by combining all of the statistics of all of the various hospitals containing a large number of average men. This will give the true average of the total surgical or medical experience. In America, we suffer from the gross inability of being able to follow up all the cases for a sufficiently long time. Part of this certainly is due to the fact that when patients do not feel themselves cured by one man, they practically invariably seek another. It would be of great advantage if a central agency could be created where the histories of all patients from all hospitals could be centered and filed. At any subsequent time any further medical event would be promptly registered and accredited to the proper history. Gradually an enormous mass of most useful information dealing with the true results of surgical therapy would be accumulated and surgical experience would derive truly accurate notions of what surgery can do. An additional value would be given to such a scheme in that the final judgment of medical events, their interpretation and value, the judgment of their various interrelationships and, especially, of end-results, and the reasons for fatalities would be made by impartial minds not biassed by the intense and uncontrollable desire to make one's own results as superlative as possible. Such a scheme would be best carried out by some central agency such as a national medical association.

There is ever recurring necessity to review all the means at our disposal for arriving at a *diagnosis in abdominal disease*. Goldie[7] points out that the rapid accumulation of new facts, theories, and tests makes it difficult to retain a sense of proportion and to guard against the tendency to fasten upon some pathognomonic sign or to seek some short-cut to a diagnosis. Of late, there have been recorded a great number of facts by workers in all branches of medicine. These have opened up new methods of approach and illuminated the stores of unapplied

knowledge, making it possible to form better conceptions of the correlations of the various portions of the alimentary canal and to build up new hypotheses to be tested by experience. Such new facts and conceptions are slow to gain a foothold in textbooks; a few of the well-known types might stand out here and there; others are exasperating in their vagueness and indefiniteness. The usual gastro-intestinal patient presents a medley of complaints, often without apparent relation, either to one another or to a common cause. A patient with such symptoms of abdominal disease needs intensive study by a number of men trained in all of these newer conceptions and ways of thinking; under such conditions, "snap" diagnoses are not possible or expedient.

Surgical therapy in abdominal disease is done on living tissue and should be considered from this standpoint. I agree with Horsley[9] that a knowledge of anatomy is essential, but merely following anatomical landmarks and making beautiful dissections should not be one's sole aim. To be sure, this is properly included but it is much more important that, besides extirpating or correcting whatever pathology is present, a restoration of the physiology of the affected organs shall take place. The physiology and pathology of living tissues and organs are the essential guides in planning any operative procedure. It is often true that a patient may recover when but little regard is paid to these considerations, but the success of an operation should not always be judged by the fact that a patient survives; and not always can one hope for such good fortune. The average eventual morbidity as well as the present mortality must be considered.

The use of *radio-active energy*[10-17] *in the treatment of malignancy* is daily becoming more important. A close student in this domain cannot fail to appreciate the fact that radio-active substances are the most powerful agents in the whole therapeutic armamentarium of medicine. The selective action of this energy when the quantity and quality are correctly adjusted presents a most remarkable phenomenon. It is still questionable whether all of the failures must be ascribed to the inefficiencies of the agent. The percentage of cases suitable for radium therapy is, possibly, as small as the number of cases suitable for radical surgery. The progress of radium therapy is intimately concerned with the construction of apparatus with tubes of the Coolidge pattern which are capable of accepting electrical energy in excess of 200,000 volts; with the determination of correct technic, especially in regard to filtration, which has brought about effective radiation; and with the establishment of fairly accurate dosages for the various kinds of tissue to be exposed to the ray.

By the preoperative application of radio-active energy, the danger of transplanting carcinoma cells during operation is minimized. It is most important that all parts of the tumor receive an even and homogeneous dose, sufficient to destroy all the cancer tissue and thus prevent recurrence. Clinical knowledge as to the location of the tumor and its biologic properties is necessary so that one may intelligently combine surgery, radium and the roentgen ray. Of 320 cases of deep-seated malignancies reported by Haggard,[12] and which were treated by various

methods, of those which had recurrences 66 per cent had only one method of treatment, whereas of those which had the combined method, only 33 per cent recurred. This seems to justify the extensive use of radio-active energy both before and after operation. Both local and meta-static conditions are most safely handled in this way.

In summing up the situation, Perthes[13] concluded that there are still many problems to be settled. At the present writing, operative mea-sures still hold first place.

Abdominal Tuberculosis.[22—46] A study of the period preceding the development of allergy after infection with tuberculosis, seems to make it evident that the local lesion resulting from the infection and the general antibodies which induce the reaction to tuberculin develop simultaneously. This is shown in the studies of Debre, Paraf and Dautrebande.[22] The tuberculin test has never given absolute satis-faction. When the general clinical picture of a patient strongly suggests tuberculosis, a negative response should generally be ignored.

The positive manifestations of a tuberculin reaction include the general febrile reaction, the focal reaction and the local reaction. A general or febrile reaction alone gives no useful information. In patients in whom a positive diagnosis can be made with some confidence upon general clinical grounds, the focal reaction is most likely to be obtained. The latter indicates the existence of a tuberculous lesion but the reaction is of much less use from the point of view of treatment. In practise, the test is indicated in few, if any, of these cases, for in the desired instances the reaction is scarcely, if ever, obtained. In Bardswell's[23] opinion, it is in the cases in which assistance is most needed that the tuberculin test is least likely to give any indication. Gibson and Carrol[24] concur in this opinion.

Gibson and Carrol[24] have taken up the Wildbolz auto-urine test in America. They explain that the test is the product of the thought that when there is an active tuberculous process in the body there must be products of elimination and disintegration of tubercle bacilli. These products are active antigens and are thrown into, and distributed by, the blood stream where a part of them are held and made harmless by the defensive mechanism and a part are removed from the organism by the excretory organs, the kidneys, the intestines, the liver, etc. The demonstration of the latter part of these antigens is a proof of the existence of an active tuberculous process in the body. I described the technic of Wildbolz's[25] method in PROGRESSIVE MEDICINE in June, 1919.

Wildbolz's auto-urine test is a tuberculin test in which the antigen is furnished by the patient himself in his own urine. If this reaction is positive, the assumption is that an active tuberculous process is present in the body. In anergic persons the test is believed to be of great value; for the urine of a person harboring an active lesion and reacting nega-tively to tuberculin, reacts positively when injected into an allergic individual, thus defining an active lesion which otherwise is impossible of demonstration.

The principles of these several theories are supported by findings in

about 300 cases reported by Wildbolz,[25] Lanz[26] and Imhof.[27] European opinion tends generally to confirm the value of the auto-urine test. The differences in results reported by Offenbacher[28] and Miche[29] are possibly explainable upon variations in technic. Alexander[31] supports the general opinion with the one exception that negative results are not always conclusive. Eliasberg and Schiff's[32] reservation is that the test does not always indicate the activity of the focus.

There is practically no American experience with the auto-urine test. From a very small experience, Gibson and Carroll[24] do not care to draw any conclusions or make any definite statements as to the value of the reaction. In none of their cases, however, were there any conflicting results. In every case in which there was definite allergy, the auto-urine test was positive.

Lanz,[26] working along the same line of thought, has presented the *auto-serum test* and reports more than 100 cases. With several minor modifications the technic is the same as that of the auto-urine test; but he believes that the auto-serum test is an improvement over the auto-urine test in that the vagaries of a diminished renal function are eliminated. The latter is an important consideration because, under marked diminution of excretory function, the antigens are highly diluted and almost impossible of demonstration in the urine while they can be shown to be present in the blood. There is also less liability to skin necrosis. After an observation with both the auto-urine and auto-serum test in over 300 cases, Lanz concludes that the reactions are the finest diagnostic medium for the discovery of an active tuberculous focus.

Gibson and Carroll[24] point out one practical advantage of the auto-urine test, namely, the extreme convenience of obtaining specimens of urine rather than of serum from young patients.

The frequency of *intestinal tuberculosis* is well shown in the figures complied by Brown and Sampson.[34] Of 19,612 persons dying of tuberculosis in the state of New York, 3.5 per cent of 603 persons were certified as having abdominal complications. Of 89 consecutive cases studied at Trudeau Sanatorium, intestinal tuberculosis was found in 6 per cent; it is found in 50 to 80 per cent of autopsies on patients dead of pulmonary tuberculosis.

The present status of the diagnosis of intestinal tuberculosis is comparable to that of pulmonary tuberculosis twenty-five years ago. The heretofore "usual" symptoms of intestinal tuberculosis are those that occur in the more advanced stages of the disease, namely, persistent diarrhea, abdominal pain, tender points in the abdomen, with or without rigidity, in the absence of an acute abdominal condition. Tubercle bacilli in the stools are of little diagnostic aid. Suggestive symptoms of beginning intestinal tuberculosis include, among others, any digestive disturbance, marked constipation, failure of the pulmonary condition to improve, an irregular temperature with subnormal fluctuations, and possible decrease of pulmonary symptoms, alternating constipation and diarrhea, marked nervousness, and improvement in pulmonary, with increase in abdominal, symptoms.

The roentgenologic evidence includes failure of the cecum, or of the

ascending colon to the middle of the transverse colon, to retain barium; the presence of spasm or filling defects; or of confirmed segmentation with, or without, dilatation of some coils of the intestine; ileal stasis or gastric retention. A general hypermotility with complete, or nearly complete, emptying of the colon in twenty-four hours usually occurs in more advanced cases.

The proportion of cases of peritoneal, to cases of intestinal tuberculosis is as 150 : 453, as determined in a series of 603 abdominal cases. The source of infection in tuberculous peritonitis is the sputum. In intestinal lesions that part of the bowel subjected to the greatest strains is affected first. Brown[36] found that 85 per cent of intestinal tuberculous lesions were at, or around, the ileocecal valve. Draper's[37] experience is that the incidence of tuberculosis in ileocecal lesions of all kinds was 3 per cent.

Gilberti's[40] experience with *chronic tuberculous peritonitis* is that mild cases may subside under expectant treatment alone and that surgical intervention is contraindicated because of the danger of depressing the general condition too much. Gatti and Gelpke[547] point out that the tubercles must be given time to develop fully before the laparotomy can have a beneficial action. Surgical intervention is most likely to succeed when the tubercles show vacuolation from a dropsical tendency. The best outlook for operation exists when the ascites is free, abundant and serous in the presence of a gradual depreciation of the general condition. Gilberti's[40] experience with the x-ray treatment is discouraging; heliotherapy, however, displayed striking effects.

C. H. Mayo's[41] experience is that surgical intervention will probably succeed if the abdominal condition is the main factor. The possibility of cure of this form of tuberculosis is due to its being confined in a cavity where it can be attacked by Nature's forces. By removing the focus of disease, especially when such a focus involves a tuberculous mucous membrane, a high percentage of cures, with a low percentage of primary operative mortality, is secured. When a mixed infection is established, the cases are more chronic and difficult to treat and control.

Echinococcus Disease.[47-49] There are a number of further reports from Italian sources concerning the intradermal test for echinococcus disease. Pontano[47] reports extensive clinical and experimental research to show that Casoni's method (intradermal injection of fluid obtained from a hydatid cyst of an animal) is a very sensitive test and proved positive in 84 per cent of the cases. The subcutaneous reaction was positive in 66 per cent. The Ghedini-Weinberg fixation of complement test was positive in only 50 per cent. The latter test does not occur when there is suppuration within the cyst. Serra[48] and Pesci[49] each confirm these observations; and both speak of the harmlessness of the hydatid fluid which is used for injection.

Roentgen-ray Diagnosis.[50-62] In previous numbers of PROGRESSIVE MEDICINE, I have covered the pneumo-peritoneal method of x-ray examination. The initial hyperenthusiasm has subsided and the true level and value of this adjuvant method is being established.

A definite technic has been adopted by the Viennese hospitals[52] as a

result of considerable experience. For several days prior to the examination, the intestines are kept well evacuated; no food is given on the day of examination and the bladder is emptied immediately preceding the examination. A subcutaneous injection of morphine is given and the patient is placed upon a movable table. He is then screened to ascertain the amount of gas in the gastro-intestinal tract. The technic of injection is that described previously in America. After the examination, a needle is reinserted and the greater part of the injected gas is allowed to escape under screen control. Spontaneous resorption does not take place for several days and in some cases for several weeks.

Le Wald[58] demonstrated that a very moderate amount of gas in the abdominal cavity is sufficient for diagnostic purposes. A proportion of 2 ccm. of gas to 100 gm. of body weight seems sufficient. Sante does not agree as to the quantity of gas to be used; for certain purposes—to delimit retroperitoneal masses—overdistension is recommended. Insufflation is of advantage chiefly in conditions difficult to recognize clinically, such as atrophic diseases of the liver, metastatic growths and small amounts of fluid. It offers no advantage in the diagnosis of disease of the gastro-intestinal tract or of the gall-bladder. Tyler's[53] experience has been that pneumoperitoneum is most helpful in distinguishing pathologic conditions on the left side, especially pancreatic cysts and the various types of splenic enlargements.

In acute perforations[63] of the gastro-intestinal tract, the possibility of demonstrating the presence of free air in the peritoneal cavity fluoroscopically should be considered. The first reference to this aid was made in 1916 by Robert Lenk, a military surgeon working on the Eastern front. Kellogg[62] refers to this aid this year. Similar possibilities are present in the diagnosis of perforation during typhoid fever as noted by Danby.

Abdominal Injuries.[63–67] Smital[63] reviews the stab and gunshot wounds of the abdomen occurring in civil life which were observed in the Hochenegg Clinic in Vienna in the last ten years. Naturally, they were mostly revolver wounds, and a large proportion showed only a wound of entry. The severe lacerations observable under war conditions were not seen; treatment of the civil wounds is, therefore, a much more limited field.

The matter of diagnosis is still more important. It can readily be made when any of the viscera protrude; otherwise, it may be difficult. Shock may be entirely absent in the civil wounds. The important point to remember is that every wound of the abdominal wall should be immediately widened to make sure it has not penetrated the peritoneum. The *definitely positive indications* for laparotomy include: (1) Extrusion of abdominal contents; (2) escape of gastro-intestinal contents, or of urine from the wound; (3) severe anemia associated with an increasing zone of dulness indicating severe hemorrhage; (4) the x-ray demonstration of air or gas in the peritoneal cavity. The *relatively positive indications* for laparotomy include: (1) Peritoneal irritation; (2) the direction of the path of the projectile through the body. The *negative indications* as regards operation are: (1) Open non-penetrating wounds; (2) a general condition indicating inevitable death.

There are still some echoes from the recent military experience which give valuable information in regard to abdominal injuries. In judging of the technic to be employed in repairing the injury, the amount of shock which is present is an important criterion. Resections of intestine ought to be avoided, as undoubtedly the additional shock may prove fatal. Even when resection is not necessary, every care should be taken to guard against any increase of the depreciated general condition (i. e., by maintaining body warmth; large incisions to minimize handling and to favor speedy operating). In extravasations of intestinal contents, simple mopping out is much better than copious lavage. Drainage is to be avoided except for the insertion of a lead down to a local septic focus or to a doubtful suture line in the colon. Lateral anastomosis is necessary when the two ends to be united are grossly unequal, when there is marked distention in the upper reaches of the gut in the presence of a peritonitis, and when a resection of considerable extent is done in the lower ileum.

I quite agree with Jonas[64] that with acute intra-abdominal lesions resulting from injury, one is not nearer to determining the exact nature of the lesion prior to opening the belly than one was twenty years ago. It is true that one has learned more fully to appreciate the danger signals and one is fully aware of their gravity, but it is not possible to distinguish between contusions and lacerations of the hollow and solid viscera nor to estimate the extent of the damage. But one has learned that when in doubt an open exploration is the safer plan.

IMPALEMENT INJURIES[548] are usually of a severe nature. Häggstrom[548] reports 5 cases from Petren's service in Stockholm. An exploratory laparotomy is indispensable whether the injury is through the perineum or anus. There are 2 other cases in the Scandinavian literature. In 1911, Silbermark had compiled 224 cases.

Elective Localization in Abdominal Disease.[68] I am much interested in Rosenow's[68] latest analysis of the results of his experimental work on infections. The subjoined table taken from his paper gives a general résumé of his experiments in the elective localization of bacteria.

ELECTIVE LOCALIZATION OF STREPTOCOCCI IN ULCER OF THE STOMACH, CHOLECYSTITIS, AND APPENDICITIS.

Source of streptococci	Strains	Animals	Percentage of animals showing lesions in															
			Eyes	Teeth	Skin	Muscles	Joints	Intestines	Appendix	Stomach and duodenum	Gall-bladder	Kidneys	Lungs	Pericardium	Myocardium	Endocardium	Nerves	Central nervous system
Ulcer of stomach	37	168	0	4	0	4	12	4	1	68	21	3	0	2	3	10	0	?
Cholecystitis	12	41	0	0	2	7	17	17	0	29	80	5	5	0	2	10	0	?
Appendicitis	17	71	0	0	0	12	29	9	70	11	1	0	0	0	9	21	0	?
Myositis	24	159	0	7	3	75	31	0	0	15	2	11	7	6	14	11	11	?
Acute poliomyelitis	22	123	0	2	0	16	15	5	2	13	2	2	11	5	7	7	4	46
Miscellaneous	71	212	4	3	4	12	9	4	1	9	1	9	7	0	4	12	4	?

I quote rather liberally from Rosenow's[68] discussion.

In view of the large number of animals injected and the wide range of the source of the streptococci, the incidence of lesions in the various organs following the injection of non-specific strains may be considered an expression of their relative susceptibility to infection. It is to be noted that lesions in the joints, the muscles, the stomach and duodenum, and the endocardium rank highest, which corresponds in general to the frequent occurrence of spontaneous infections in these structures in man and animals. The relatively high incidence (21 per cent) of lesions in the gall-bladder following the injection of the ulcer strains, and in the stomach and duodenum (29 per cent) following the injection of the gall-bladder strains suggests a basis for the common association of two or more of these conditions in human pathology. The experiments further suggest that initial foci in the tonsils and teeth must be important factors in the production (persistence, I should think) of abdominal disease. A focus of infection that is teeming with organisms wherever found, should be regarded as a test-tube with permeable walls embedded in the tissues; the continued growth of living bacteria and their products ultimately tends to break down the protective mechanism of the host.

This suggests the careful elimination of such foci as a prophylactic procedure. The benefits should be especially noticeable in preventing acute exacerbations in chronic conditions. The elimination of visible foci, however, will not prevent all of these infections.

In this association one can speak of the typhoid carriers. Typhoid fever under such conditions is an experiment in the elective localization of bacteria. Originally lodging in the intestine, the infection frequently thereafter shows a predilection for settling secondarily in the bile passages notably in the gall-bladder and cystic duct. (There are, of course other localizations especially the bones; I confine my remarks, however, to abdominal disease.) According to Henes, the bacillus typhosus is the initial infecting agent in the gall-bladder. In clinical experience, this infection may occur years after the primary fever had disappeared. Evidently, we have all the factors in the experiment: an initial focus capable of providing typhoid bacilli; a secondary focus in which these may lodge and continue to grow with, or without, acute exacerbations.

I might speak of other illustrative facts in clinical medicine: the pneumococcus and lobar pneumonia; the amœba coli and dysentery, etc. Lastly comes some new experimental work of Mann[465]—rather unexpectedly stumbled upon—which shows that under certain conditions a similar course of events may follow chemical stimuli. A rather broader illustration along similar lines lies in the effect of histamine on the circulatory system as in the experiments of Dale, Richards and Laidlaw on the subject of shock. Perhaps, this should not be surprising inasmuch as the mechanism whereby bacteria act is undoubtedly a chemical one.

In sober thought one cannot escape the conviction that in human pathology there must be constantly going on an elective localization of areas, organs or tissues by the causes provocative of disease. There

must necessarily be a combination of (1) sufficient virulence of the infective agent or cause; (2) a lessened resistance upon the part of the whole animal organism; and (3) certain local changes either of nutrition and blood supply or of destruction of tissue, which establishes an area more favorable for the lodgment of the foreign agency. Then disease appears. In a general way one can distinguish that such changes go on constantly; fortunately in the great majority the recuperative powers of the animal organism are so marked that these insults are quickly repaired, even, perhaps, without disturbing the ordinary routine of the animal machine. It is equally true that in certain organs or areas the nature of the various components normally present may predispose to the changes noted previously which tend to the formation of states of impoverishment of normal resistance necessary for the growth of certain bacteria more frequently than in other areas or organs. Circumstances of this general kind probably form the physical basis for the elective localization that bacteria show. Except for general notions of this kind we have no more precise knowledge.

Local Anesthesia in Abdominal Surgery.[71-80]   About 143 communications have appeared on the subject of *blocking the splanchnic nerves.* I reviewed this subject last year and described the two forms of technic —that of Braun and that of Kappis. Preiss'[71] conclusions are that the preferable technic is to inject the anesthetic on a level of the third lumbar vertebra, instead of Kappis' lower site. A secondary injection can be made from the front, after the abdomen is open, to supplement the original Kappis technic. The pricking of a vessel does no harm, but the injection of the anesthetic solution into the lumen of the vessel may be serious. Preiss' experience consists of 192 cases; he is impressed with the excellent postoperative condition; and the dangers seem no greater than with ordinary forms of anesthesia.

Most of the reports in the literature are from foreign sources. Widere and Borchgrevink[72] prefer Braun's technic and have employed the method in operations upon the stomach, gall-bladder and intestines. Over 200 cases have been so anesthetized in Braun's clinic. Reports from other clinics do not agree as to the favorability of the method and some of the reports are discouraging. Buhre[73] advises the Kappis technic and prevents bad results—death, collapse, etc., by blocking the nerves after opening the abdomen. Naturally, the abdominal wall must be anesthetized separately. This seems to be the technic employed by Carulla Riera.[74] Billet and Laborde[78] seem to think that the only danger comes from the puncturing of the renal vein.

Labat's[76] technic is very typical and seems good. It consists of local infiltration of the abdominal wall followed by splanchnic injections. The abdominal part of the technic is the following: Five anesthetic wheals are raised (1) at the tip of the xiphoid; (2, 3) one on each side at the level of the tenth costal cartilage where the exterior border of the rectus crosses the costal margin; (4, 5) one at each side on the external border of the rectus a little higher than the umbilicus. The needle, which is 8 to 10 cm. long, is passed through each wheal and the infiltration is made fanwise. The deep layers should be infiltrated first, and

the superficial layers later. The solution is also injected within the rectus sheath. This is quite sufficient to anesthetize the peritoneum and gives good relaxation. For the splanchnic anesthesia the patient lies on the side and the site of injection is four fingers' breadth, or 7 cm., from the midline of the back, just under the lower border of the twelfth rib. The needle is introduced obliquely forward so that it makes an angle of 45 degrees with the median plane. Its point then strikes the bodies of the vertebræ near the anterior convexity behind the splanchnic nerves just where they join the semilunar ganglia. When the needle, having been introduced for about 9 cm., strikes bone, it should be made to pass tangentially to the latter one centimeter further and after making sure that no blood comes out of the needle, 25 or 35 cc of solution are injected.

A novel form of local anesthesia is proposed and described by Baruch.[77] Instead of blocking the intercostal or lumbar nerves or the celiac plexus, Baruch[71] makes a subumbilical injection of 600 cc of 0.25 per cent novocaine-adrenalin solution into the abdominal cavity by means of a cannula needle. In 2 cases good anesthesia of the parietal peritoneum was established, but the effect on the viscera was unsatisfactory. Baruch[77] recommends further experimental work with larger injections and a stronger solution as after the abdomen is opened a considerable amount of the solution drains away. This method should be accepted or discarded in the light of an observation made by Bartlett[79] that 6 ounces of a 0.5 per cent solution of novocaine poured into the peritoneal cavity of a 15 pound dog caused death from respiratory failure in about twenty minutes.

In discussing the general subject of local anesthesia,[80] as it relates to abdominal surgery, Farr[80] discusses the real, as well as the imaginary, shortcomings of the method. One of the objections most frequently offered relates to the psychic effects of an operation performed upon a conscious patient. Most of this is due to (1) the precedence of general over local anesthesia for the last sixty years; and (2) the lamentable fact that so large a percentage of operations performed under local anesthesia are done under " a technic which leaves the patient no choice but to become an active anti-local propagandist." Another shortcoming in abdominal work is that under local anesthesia thorough general exploration of the abdominal cavity is usually impossible, even though visualization of the organs in the immediate neighborhood is possible. A third inconvenience is the hardship upon the surgeon and the distraction of a part of his interest from the actual operation. A fourth is the element of time. A fifth is the contraindication of childhood. Farr[80] tries to make out that most of these are imaginary shortcomings.

I am in sympathy with all of the statements which Farr[80] makes in regard to the use of local anesthesia in abdominal operation, but there is no gainsaying the fact that local anesthesia, as usually practised both here and abroad, is not the method of a humane choice but rather of a stern necessity. When all other circumstances are equal, the ideal method of conducting an operation is with the patient under the influence of an anesthetic; nine patients out of ten will agree with this statement—

and, after all, theirs is a most important opinion. Anyone who does any operating will readily agree that, in the strict sense of the word, there are no advantages to local anesthesia; one practises this method to avoid disadvantages that are inherent in methods of general anesthesia, or to avoid increasing the dangers of a severe illness, or to prevent certain complications which are said to result from the drug employed, or from the inhalation method of administering the latter. Only for these reasons are methods of local anesthesia used. (Naturally, I do not refer to small minor operations.) To speak of another reason, namely, the incapacity of young and ill-trained, or not sufficiently trained, anesthetists, serves only to bring up the question of the exigencies of our customs in the training of medical men.

There are few conditions which absolutely forbid the use of a general anesthetic when it is intelligently given by an expert. Many of the contraindicating conditions which have to do with the circulatory mechanism are better handled with judicious general anesthesia than by the use of local anesthesia; many others referable to the kidney can be handled by avoiding those agents which have poisonous effects on the renal parenchyma; for such gas and oxygen is an ideal anesthetic. I have the impression from my own experiences that in many of the cases an unfortunate outcome is not the result of the anesthetic, either general or local, but of the initial disease and its grade of severity, or of other accompanying pathologic states which make the resisting power of the individual of too precarious a nature to successfully withstand any operative insult. For the very few, for whom local anesthesia in some form seems imperative, every advance and betterment in the technic of local or regional anesthesia is a highly desirable item; such patients need every safeguard which surgical technic can afford.

Postoperative Complications.[81-92] Moutier[84] reports 3 cases of acute POSTOPERATIVE ESOPHAGITIS. These were in women who had swallowed much of the fumes of the anesthetic. The signs, intense salivation and lacrimation, severe pain in the esophagus and dysphagia—developed in about twenty-four hours and reached their height on the fourth day; they subsided by the end of the week.

Severe POSTOPERATIVE SINGULTUS[85] is an uncanny complication. Kuttner[85] reviews a group of 12 cases. The condition usually appears on the day of operation or the following day, lasts several hours, then stops and then begins again without assignable cause. It is not affected by diet, by the position of the patient in or out of bed, nor by his movements; sometimes speaking seems to precipitate an attack. A severe form of this phenomenon weakens the patient and can be a contributory cause of death (Marion). It is most frequently seen after abdominal operations. One is almost powerless in the face of the severe form of singultus. (Many of these are caused by a diaphragmatic pleurisy. Reviewer.)

ACUTE POSTOPERATIVE DILATATION OF THE STOMACH[86-87] seems to be of greater frequency than is usually supposed and, being often unrecognized, is a potential source of serious harm and even death. Cases of this kind appear in the literature under a confusing variety of names:

arterio-mesenteric ileus, acute paresis of the stomach, gastro-duodenal dilatation or ileus, etc. Of 92 postoperative cases reported by Broch-gevink, 71 occurred after laparotomy, but only 31 of these were after operations upon the gall-bladder, appendix, or stomach (in the order of frequency). About 60 per cent of the cases are in women.

The clinical picture produced by this condition is fairly distinctive. The most prominent symptom is vomiting. This, in a large proportion of cases, becomes conspicuous soon after operation although the onset can occur many days later, perhaps long after the patient has recovered from its immediate effects. The vomiting is characteristically of a regurgitant type, the gastric contents being spit up, as it were, with little retching or straining. The vomiting gives little or no relief, and appears to be only an overflow from the stomach. Most frequently the vomitus is green or brown but, in the later stages, it may become almost black. The large amount of total vomitus, far exceeding the fluid intake, is very characteristic.

Pain is almost always a negligible symptom and most often amounts to only a feeling of distress in the epigastrium. Collapse is noted in practically all severe cases.

Of the objective signs the most characteristic is distension of the abdomen. The introduction of a tube is immediately followed by the escape of much gas and fluid with the prompt collapse of the stomach and disappearance of the abdominal distention.

Cases are reported in the literature (Doolin,[549] Lee,[548] Novak[86]) in which the phenomenon was observed on the operating table: in Doolin's case, recovery followed the immediate evacuation of the stomach contents; in Lee's case, death followed within a few hours.

There are two prominent theories as to the etiology of this condition: (1) The theory of duodenal occlusion by the upper border of the mesentery with its contained vessels; and (2) the theory of muscular paralysis. All in all, Novak,[86] from whose paper this information is taken, feels that the weight of evidence is in favor of the paralytic theory—that this, more than any other, explains the varied immediate etiology of the condition and that it alone seems to explain those rapidly occurring dilatations occasionally observed during laparotomy.

The two important therapeutic measures are gastric lavage and the postural treatment. Novak makes no mention of the insertion of a duodenal tube for permanent drainage; and makes light of any operative measures. In other quarters gastro-enterostomy has been recommended with no very brilliant results.

The FREQUENCY OF LUNG COMPLICATIONS, according to Mandl,[88] in abdominal operations (especially those upon the stomach), depends on the character of the manipulations rather than on the mode of anesthesia. The pulmonary complications are most frequent after resections. It was notable that the farther away the operated area was from the upper abdomen (I should rather say, from the diaphragm) the less frequent were the lung complications. (This is a well-known factor. Reviewer.) Chilling of the patient seemed an important factor to Mandl, and was shown by the marked increase in lung complications

during the winter of 1919–1920, when, owing to the scarcity of coal, the operating rooms and wards could not be adequately heated. This is in marked contrast to the experience of a large hospital to which the reviewer is attached; most of the lung complications there occur during the late spring and beginning summer. Mandl recommends the prophylactic use of digitoxin; with this measure they were able in Hochenegg's service to reduce the proportion of cases from 27 to 8 per cent. The effect is explained by Mandl on the basis of the reaction of the pulmonary vessels and the changes in the blood distribution. v. Jaschke[89] confirms this opinion. He believes also that scrupulous hemostasis is another factor.

Scrimger[90] reports 7 cases in which total collapse of the lung was observed within a few hours after operation. The patients all recovered.

SURGERY OF THE ABDOMINAL WALL AND PERITONEUM.[93–99]

Tumor of the Abdominal Wall.[93–95] Klot[94] has compiled 408 cases of tumor of the abdominal wall. The list includes:

Fibroma	248 Cases
Fibrosarcoma	67 "
Fibromyxoma	17 "
Sarcoma	60 "
Endothelioma	1 Case
Angioma	1 "
Angiosarcoma	1 "

Recurrences were observed in 38 cases all but 6 of which were sarcoma.

The question as to **how often the symptoms present with an epigastric hernia**[95] **are due to the hernia** *per se* and how often they are due to intra-abdominal disease is not a new one. Many surgeons are still quite satisfied to deal with the hernia itself. Lewisohn[95] debates this subject and points out that the relief which the patients experience is true only in a certain—not too large—percentage. The frequency of the co-existence of intra-abdominal lesions with epigastric hernia is by no means small; he has had an experience of 13 cases in four years.

I heartily agree with Lewisohn that experience has shown that small incisions are not in the interest of the patient when dealing with an epigastric hernia, but that the surgeon should make an incision large enough to enable a thorough exploration of the intra-abdominal organs at the same time that the hernia is to be repaired; reoperations will then be avoided.

Peritoneal Absorption.[97–98] The subject of peritoneal absorption has a practical interest for surgery. Clark[97] goes extensively into the mechanism of this phenomenon when there is an appreciable difference in the osmotic pressures of the introduced fluids and the blood or lymphatic streams. Clark, however makes no attempt to explain the absorption of fluids which are in complete equilibrium with the blood, such as serums, or artificially made solutions or mixtures of equal osmotic pressure. Inasmuch as these are absorbed, the mechanism is undoubtedly much dependent on physiologic processes which have to do with

the supply and demand for fluids and solids in the various tissues of the body.

Intraperitoneal Infusion. Weinberg[113] reports that intraperitoneal infusion is a simple, harmless and very effectual method of delivering water to infants and may, in properly selected cases, be superior to subcutaneous infusion in dealing with a marked loss of fluid. The opportunities for resorption are excellent and the procedure is exceedingly rapid. The shock effects are slight. According to Denzer and Anderson,[104] absorption of fluid, injected into the peritoneal cavity, occurs in from twelve to forty-eight hours. Saline solution causes a temporary reaction—a sterile inflammation.

In disease accompanied by *ascites*[105-107] the normal physiologic mechanisms are naturally disturbed, either because of overactivity of the secretory activities, or because of interference with the processes of absorption. Up to the present, the processes of secretion have been beyond our influence and any therapeutic endeavor toward the alleviation of abnormal accumulations of fluid within the peritoneal cavity must be directed with the object of aiding or increasing the powers of absorption. In a general way, some of the attempts are fairly similar to those technics invented for the continual absorption of fluid from other hollow spaces: these generally include the formation of a drainage passageway to the subcutaneous areas.

Huber[105] reports the case of a boy, aged eight years, in whom the Lambotte-Handley plan of drainage was used with good result; the strands of silk were led out to the subcutaneous region of the thigh and the anterior abdominal wall; the case was followed for four months.

Glass drains have also been used for this purpose; these suffer from the disadvantage of being breakable and of being foreign bodies which become encysted. Huber notes that calf aorta, hardened in formalin, does not act as a foreign body.

In 2 cases of hydroperitoneum, Behan[106] made use of sections of paraffined veins which, having been fastened to the peritoneum by a technic similar to that used for the implantation of a ureter, were led out into the perirenal fatty tissue or into the retroperitoneal cellular tissue or into the subcutaneous layers of the abdominal wall. Both patients were very greatly relieved. Behan has found it possible to preserve varicose veins, removed at operation, for this purpose; the veins are threaded over glass rods and are hardened and paraffined with the same technic used in the pathologic laboratory for the sectioning of tissues.

A much better operation along these same general lines is that employed by Griffith[107] in 8 cases of cirrhosis of the liver with ascites. Cases of this nature with minimal cardio-renal involvement seem ideally suited for Griffith's operation. The technic can be carried out under local anesthesia and is as follows: The major saphenous vein is dissected free for a distance of eight or nine inches from its point of emptying into the femoral through an appropriate incision. A second incision, having been made above Poupart's ligament, a passageway is bluntly dissected subcutaneously from the first incision and the liberated

vein is brought through and up the artificially made canal. The end of the vein is sutured to an opening in the peritoneum with fine silk.

The Peritoneum.[97-99, 108-131] The subject of PERITONITIS[108-131] is one of such vast importance that it does not suffer from being repeated from time to time, even though its salient features are probably familiar to everyone. The question of *chemical and mechanical peritonitis* is one around which considerable discussion has centered. The term, according to Murphy, is a convenient one for those instances in which typical peritonitis is produced by supposedly sterile substances, such as the contents of a cyst. Deaver[109] is inclined to believe that this form also is infective, inasmuch as the excoriation of the endothelium prepares the way for the entrance of pathogenic organisms in much the same way as the twisting of the pedicle of a cyst. Blood, bile and urine, even if uninfected, will excite an inflammatory reaction—the last two being expecially irritating—and favor the introduction of bacteria. In the presence of a perforated viscus, the blood, bile, or urine may already have been infected.

The subject of *bile peritonitis* has been reviewed several times in PROGRESSIVE MEDICINE and is referred to again in this year's literature by Donovan.[550] General and localized forms of peritonitis occur. Frequently no perforation of the biliary passages is demonstrable. The prognosis is generally fair when the condition is promptly drained.

In regard to *the bacterial flora of peritonitis*[109] it is recognized today that this is nearly always a mixed infection; the most important organisms are staphylococci, streptococci, colon bacilli, pneumococci and gonococci.

The importance of the colon bacillus is generally recognized, although the idea that every peritonitis of intestinal origin is due to this organism exclusively is not supported by the facts. The error is explainable on the well-known tendency of the colon group of organisms to increase most rapidly and to overgrow the other associated organisms. Experiments were undertaken by Gál to ascertain whether it is possible to influence infectious inflammations of the peritoneum by means of the colon bacillus. It was shown that in guinea-pigs an induced peritonitis can be cured for the most part by an autolysate of colon bacilli. The autolysate exerted no particular influence on the opsonic index, but it induced a leukocytosis and a more marked phagocytosis of various bacteria in the abdomen and thus indirectly counteracted the toxicity of the bacteria. The great omentum was the main site of the conflict. How far these laboratory observations may be applicable to human disease remains still to be shown by clinical investigation.

Streptococcic peritonitis[109] occurs more frequently in women than in men because of the greater frequency of that organism in pelvic infections of the female. When due to the latter, as in a puerperal infection, the peritonitis is really a retroperitoneal phenomenon. Polak[111] is led to believe that nature is competent to localize such lesions. In an advancing process, however, with a definite symptom-complex, drainage is necessary; the latter is best done through the vaginal fornix.

A form of *streptococcic peritonitis*[109] is occasionally reported in which

the peritoneum becomes inflamed *without concomitant involvement of any of the abdominal viscera.* The infection is blood-borne and is probably derived from the nasopharynx (tonsils). The relationship of this type of peritonitis to epidemic sore throats has been suggested by observations made during epidemics of this character. The cases observed show a tendency to affect female children.

Primary pneumococcic peritonitis[113-116] is not common, although cases seem to be reported with increasing frequency. It is a fatal form of infection, unless localization of the process quickly takes place, and occurs more often among female children also. According to Hertzler, the secondary form of pneumococcic peritonitis occurs in about 1 per cent of all pneumonias.

Heiman[113] contributes the latest study of pneumococcic peritonitis. In a five year period at Mt. Sinai Hospital, the pneumococcus was isolated only 15 times in 125 cases of peritonitis of all kinds in children. Type I was present in 5 cases; Type II, in 1 case; Type IV, in 3 cases. Blood cultures were positive in 5 of 8 cases. A high leukocyte count was characteristic. The course of the disease is divided into three stages: (1) A sudden onset with severe abdominal pain, usually generalized but most marked in the lower right quadrant; rise of temperature with rapid pulse; prostration. Abdominal rigidity is not so marked as ordinarily. Signs of fluid are often elicitable. (2) A phase of improvement in the condition. (3) The terminal stage characterized by circumscribing tendencies with the attempted or consummated development of a mass in the umbilical or hypogastric regions. The temperature runs an intermittent course. Strength is gradually lost from the toxemia. Death results; or recovery follows spontaneous rupture through the abdominal wall or after operation. This description follows that generally read in the literature. Heiman made the diagnosis in suspicious cases by practising abdominal aspiration after the method of Denzer (PROGRESSIVE MEDICINE, June, 1921). The prognosis depends upon the ability of the inflammatory process to localize.

Antipneumococcus serum was used in 4 of Heiman's cases, but with no avail. The best treatment is to give abundant fluids and to wait for the acute stage to pass and for localization to occur; if no signs of improvement are apparent, it is best to resort to surgery.

In the discussion of Heiman's paper, Holt[114] referred to one type in which the peritonitis is part of a general pneumonitis, in which it gives no clinical signs, and which is found only at necropsy. At the Babies Hospital only 9 cases of a total of 171, were proved bacteriologically to be due to the pneumococcus. From a study of these, Beaven[116] concluded that in at least 7 of the 9 the infection originated in the lungs.

Gonococcus peritonitis[109, 117] is, probably, the most clearly defined type originating as it does from an infected Fallopian tube and being marked, clinically, by a stormy onset and early localization in the lower abdominal cavity, usually on one side.

By far the most frequent avenue by which the peritoneum becomes infected is from *perforation* of some intra-abdominal viscus—the most common, of course, being the appendix. Drechter[117] points out that

when the seat of the infection lies near the posterior abdominal wall, the rigidity may be most marked in the latter aspect of the abdomen.

There is much good in Deaver's opinion that operation in a case of acute diffusing peritonitis after the first thirty-six or forty-eight hours does not conserve the best interests of the patient. When the peritonitis is the result of intestinal obstruction, gastric, gall-bladder or intestinal perforation, operation should be immediately undertaken. As a general rule, the longer the peritonitis is present, the graver is the outlook. Too thorough operation in peritonitis very often spells death. As little as possible should be done consistent with doing what is absolutely necessary.

From foreign sources comes the recommendation of Lawen[118] concerning the advantages of *irrigating the abdominal cavity in cases of peritonitis*. The majority opinion in America contradicts this recommendation as an unnecessary interference in a most severe lesion and as tending in the maximum degree toward spreading the infection.

The *ether treatment of peritonitis* was first recommended during the war. Lienhardt[119] tried this method in 101 cases of peritonitis in civil practise; 1 instance of collapse occurred; a mortality of 18 per cent. A few other surgeons have had similar experiences. The procedure seems to tend to reduce the temperature and to stimulate leukocytosis; it has a striking analgesic effect. The principle advantage is the reactive inflammation and exudation which pours out antibodies on the infected surface. The local chilling from the ether is said to stimulate the bowel to contract and thus it promotes peristalsis and circulation. The great drawback is the development later of adhesions and bands. A significant fact is that the ether treatment is recommended only for the severest cases.

Neudorfer[120] treated 22 cases in this manner; there were 17 recoveries and 5 deaths. A disturbing fact is that among those who died, 3 had recovered from the general peritonitis. Another died from a residual abscess and the last from pneumonia. The number of secondary abscesses in those that recover was very striking. I have the impression that these accidents have something very intimately to do with the method of treatment.

A paralytic ileus during the course of a peritonitis may be partial or complete. *Intubation for intestinal drainage*[122–127] under these conditions was first introduced in England by Paul,* in 1891, and in America by Mixter, in 1895. Since then, enterostomy has been recommended by many surgeons. Enterostomy is useful only in the incomplete cases of paralytic ileus; when the condition is complete no treatment is efficacious.

Most of the reports this year are from foreign sources; the procedure seems to be growing in favor in Europe. In Bircher's[122] opinion the indications for enterostomy are broader than is generally believed and oftentimes no time should be wasted in performing the operation. The decision as to the proper moment for operation seems to be the chief difficulty. Of great importance from the standpoint of prognosis is the

* See, under intestinal obstruction.

manner in which the intestinal fistula functionates; the continuous and free passage of gas and fecal material is a favorable sign. If the fistula established at one point fails to answer the purpose, another at a second point may be justified. In a number of Brunner's[126] cases an opening was made at several different points before the desired effect could be produced.

Aievoli[127] has compiled 22 cases from the Italian literature. Enterostomy seemed to be a decisive factor in the recovery of 12 cases. Dubs makes a similar report in 24 other cases. The latter reports that the relief from the pain is so great that even in hopeless cases enterostomy may be advisable. Brunner has had 10 cured cases out of a total of 34 in which enterostomy was applied as a last resort. These are representative statistics—a mortality of from 25 to 50 per cent depending upon the various factors involved in so severe a lesion as a general peritonitis.

The fistula heals spontaneously when the intestine is sutured to the peritoneum; the fistula persists and requires operative closure when the intestine has been sutured to the skin.

Segagni[128] refers to a subacute form of *peritonitis with simple plastic formations* of various size and depth (reviewed two years ago). At times this form of inflammation assumes an acute phase suggesting suppuration. The natural tendency is toward a spontaneous cure. The clinical picture includes an acute onset with symptoms suggesting a severe peritonitis; soon the latter become attenuated, and then large doughy masses can be palpated within the abdomen. These shift about and are tender, but in about one month's time they can no longer be distinguished. The usual course of the disease in Morquio's cases extended from one to three months. This form of peritonitis seems to be a clinical entity rather infrequent in early childhood. The nature of the infection is not known; according to the Italians it is not tuberculosis.

Peritonitis in typhoid fever without perforation is a rare complication. Svartz and Hanson[129] report such a case in which the peritonitis developed apparently from the spread of infection through an intact intestinal wall. Between 40 and 50 of such cases have been reported in the literature. A little less than one-third were of the fibrinous variety, a similar number were purulent and the remainder were of the serofibrinous variety. Typhoid bacilli were demonstrated in the peritoneal effusion in 4 cases.

The formation of *peritoneal adhesions*[135–139] is one of Nature's methods of healing intra-abdominal lesions and one of the essentials for success in operations performed in the belly. Yet, as every one knows, they form a source of danger, and the best abdominal operative technic aims to minimize their formation as much as possible. Behan[135] shows that for the formation of adhesions between adjacent areas of bowel, or between the bowel and the other viscera, or the abdominal parietes, the opposing surfaces must be partially or wholly denuded; if one of the opposed surfaces is not denuded the latter must remain in intimate contact for a considerable length of time. If both surfaces are denuded, only a short interval is necessary for adhesions to form. Union does

not occur if there is sufficient constant movement between the opposed surfaces to inhibit intimate contact for the required length of time.

Chemicals, such as tincture of iodine or Dakin's solution and strong solutions of mercuric chloride, cause the formation of adhesions by destroying the frail endothelium of the peritoneal surface. Drying of the serosa by exposure does not ordinarily result in adhesions. Lanolin and boric acid do not prevent the formation of adhesions when a normal inflammatory reaction, due to bacterial infection, is present; they retard their formation only in the absence of the latter. They do not always prevent the adhesions when adjacent denuded surfaces are kept in contact, or when blood is present between immobile surfaces. No ill-effects were observed to follow the use of these substances, and they greatly diminish postoperative pain. To prevent the formation of adhesions, Behan recommends changing the patient's position frequently after operation and to exhibit drugs which stimulate the peristaltic activity. Tympanites should be treated immediately with heat.

Naegeli[136] investigated the frequency of intra-abdominal adhesions in 148 old laparotomy cases. They were found in all but 30. I agree with Naegeli that there is great danger of ascribing to them symptoms due to other causes.

Zucola[140] has compiled 46 cases of *cystoid pneumatosis* of the peritoneum[140], [141] from the literature. The intestines and the parietal peritoneum usually show signs of inflammation. In 25 cases there was a tuberculous peritonitis; in 7, benign processes in the stomach and intestine; in 5, septic ulcerative processes of various kinds; in 2, gastric cancer; in 2, gastric ulcer; and in 2, severe colitis. In 21 cases in which the pneumatosis was a necropsy surprise, in 9 there was tuberculous peritonitis, or lung disease, or enteritis; in the others, chronic kidney or heart trouble; and in 2, appendicitis. A very few men have reported a complete cure after simple laparotomy; Winands, by treatment of the meteorism by puncture. In all the others no benefit was obtained by treatment or the condition was aggravated. Steindl recovered a pure culture of anaërobes from such cysts studding the intestine. These must get into the lymph vessels through bowel erosions and single cysts result from dilatation of these lymphatics.

SURGERY OF THE INTRA-ABDOMINAL VISCERA.

The Bloodvessels.[142-161] There are 16 cases in the literature since 1910, including one of Chalier and Morenas,[124] of a PROFUSE SPONTANEOUS HEMORRHAGE INTO THE PERITONEAL CAVITY from a varicose vein on a uterine fibroid. The clinical picture was similar in all of them; it included a woman in good health approaching the menopause; a sudden severe abdominal pain with a tendency to syncope; the menstrual flow not abnormal in any way; and symptoms of an acute internal hemorrhage. In one case of intra-abdominal hemorrhage Hellendall[143] noted discoloration in the umbilicus which proved of diagnostic import; an umbilical hernia was present.

Astley Cooper did the first operation of LIGATION OF THE AORTA one hundred and four years ago, and the operation has been performed about 19 times since, but in no case has it been successful in man. Death has always followed in from a few hours to a few months from shock, hemorrhage, infection or something directly connected with the operation, except Hamann's case which died from hemorrhage from a bed-sore. In the case reported by Vaughan[147] this year, the occlusion was not made quite complete. The essential technic, as employed by Vaughan, was as follows: The peritoneum was opened, the aorta exposed and a piece of cotton tape, one-half inch wide, was carried around the vessel about two inches above its bifurcation and just below the origin of the inferior msenteric artery. Two turns of one end of the tape made the surgeon's, or friction, knot, which was drawn gradually tighter and tighter until pulsation was no longer perceptible in the iliac artery and barely so in the aorta, then the knot was completed, the ends of the tape cut off and the abdomen closed.

In 5 of the 20 cases mentioned in Vaughan's[147] article, there was no ulceration, and in none of the 5 was there complete occlusion of the lumen of the aorta; and these were the only patients, excepting Keen's, who lived long enough to give any expectation of complete recovery from the operation. Tillaux's patient lived thirty-nine days, Halstead's 2 patients forty-one and forty-seven days respectively, Hamann's six months and two days; Vaughan's patient is living and working one year and four months after operation.

Hesse[148] has compiled and summarized the 73 cases of THROMBOSIS AND EMBOLISM OF THE ABDOMINAL AORTA on record. Nearly 95 per cent of them died under expectant treatment. In 10 per cent an attempt was made to remove the obstruction. It was successful in 50 per cent. Embolism is more common than thrombosis and it is usually secondary to an endocarditis, principally of the mitral valve; a ball valve thrombus in the auricle is common. The symptoms are referred to the legs at first as the circulation becomes shut off from the latter. If there is no abdominal pain and no bladder symptoms, the embolus is probably at the bifurcation of the aorta. In over a half of the cases the embolus projected into the iliac artery. Transperitoneal aortotomy with extraction of the embolus is advisable in recent cases of embolism. If the blood stream becomes obstructed again after the embolus is removed and gangrene of the lower extremities develops, high amputation is, of course, necessary. In cases of thrombosis no attack is effectual at the vessel itself; the only available treatment is amputation when gangrene develops. In any case the prognosis is always very grave.

Weiss[149] has collected 55 cases of ANEURYSM OF THE HEPATIC ARTERY. This is 12 more than the total reported last year by Kading and reviewed in PROGRESSIVE MEDICINE. Rarely are tumor or bruit present and then only in the terminal stages. Under most favorable conditions ligature is indicated.

In over 4100 autopsies performed at the Massachusetts General Hospital, ANEURYSM OF THE SPLENIC ARTERY was found 3 times. Garland[150] has compiled 17 cases from the literature. The most recent

full report by Hogler was reviewed last year in PROGRESSIVE MEDICINE. Hogler was the only one who was able to make the diagnosis during life.

Considering its importance from the standpoint of prognosis and treatment, the subject of MESENTERIC VASCULAR OCCLUSION[152-156] has received comparatively little attention in the literature. The communications of Fernandez Martin,[154] Loop[153] and Klein,[152] appearing this year, are of timely interest. The contribution of Jackson, Porter and Quinby, in 1904, and Trotter's monograph, in 1913, are the most comprehensive studies available. Trotter was able to collect 373 cases. French, Italian and German writers have given the subject more attention than have the English-speaking workers. The condition is apparently not so rare as one is led to believe.

There appear to be two well-defined forms: (1) A primary form in which the occlusion is independent of any other intra-abdominal lesion; (2) a secondary form in which the occlusion occurs as a complication of various septic processes within the abdomen, usually several days after operation; or it is associated with one of the common forms of intestinal obstruction. Clinically, symptomatically, and experimentally, the cases can be further divided into the fulminating, and those of slower, more insidious development. Either of these two latter types, in turn, may appear as primary or secondary phenomena.

Experimentally by various disturbances of the blood supply of the intestines—either by ligation or the injection of foreign substances—there may be produced lesions varying from limited necrosis of the bowel wall, to extensive infarctions. Clinical observation and experiments reported by Nazarri, Schley, Karder, and others, go to show that, in man, closure of the superior mesenteric artery may be followed by (1) a complete reëstablishment of the circulation which may, or may not, persist effectively; (2) by intestinal obstruction without infarction owing to an insufficient blood supply for adequate function; (3) by intestinal infarction of varying grades, severity, and extent.

The conditions found at operation are usually characteristic. A considerable amount of free fluid—clear and without flocculi, odorless, slightly sticky, and from light straw to dark amber in color—is usually present. The involved intestine is dark red or cyanosed, soggy and lifeless. In some, the bowel presents segments with small oval areas of almost complete necrosis. Cases with massive gangrene are common. The mesentery supporting these coils of intestine is likewise thick, heavy, and waterlogged.

Mesenteric vascular occlusion is a disease of adult life. In Trotter's series, 64 per cent were in males; in Loop's series, only 43 per cent. The existence of possible sources of emboli is important in considering the diagnosis. The symptoms of greatest significance are (1) incomplete intestinal obstruction—small ineffectual bowel movements; (2) the slight degree of muscular rigidity as compared with the abdominal pain; (3) moderate distention without tympany; (4) the absence of pulse or temperature reaction except after the development of a peritonitis; and (5) the self-limited vomiting. The presence of blood in the vomitus and stools, unless otherwise explained, is another very valuable sign.

The prognosis is bad. The mortality varies from 71 to 94 per cent. Even when operation is done early, an extension of the process is quite possible.

The treatment is entirely surgical, and comprises wide excision of the affected loops and either anastomosis or enterostomy. The important thing to remember in this condition is that, although the bowel does not appear so badly damaged, it can live with its blood supply cut off. No matter how extensive the excision, it must be dealt with on the basis of a complete operation.

A feature of unusual interest in the case of mesenteric embolism reported by Block[156] was that the patient was a true hemophiliac. This treacherous complication was combated by a prompt transfusion of blood.

MESENTERIC DISINSERTION[155] following contusion of the abdomen is rare and Sencert[155] was able to find only 30 cases of this lesion on record. The lesion was associated with other abdominal injuries in from 70 to 75 per cent of the cases. The disinsertion usually occurs in the terminal ileum in about 75 per cent and in its upper segments in 25 per cent. The length of intestine usually comprised is from 10 to 40 cm. The immediate consequence of the trauma is hemorrhage which may be severe enough to quickly cause death; the ultimate effect is gangrene of the bowel for the distance disinserted.

The symptoms may be of three types: (1) A syndrome of internal hemorrhage and acute anemia; (2) a complex of an acute peritoneal lesion, especially if tearing of the bowel is also present in addition and hemorrhage is inconsiderable; (3) a rather benign group of symptoms which, however, usually mask a much more serious condition because the loop which is torn away is sure to undergo gangrene.

Operation is the only avail. Several years ago, in PROGRESSIVE MEDICINE, I referred to some experiments in which this lesion was artificially produced and was prevented from becoming fatal by wrapping the isolated loop in the omentum. Confirmation of this report appears in the work of Toracca[157] this year. In several autopsy cases in the literature it was seen that this method of repair was attempted by the natural forces. In operating upon such cases, it might be advisable to keep this fact in mind and an attempt might be made to repeat this experimental work in the endeavor to do a less shocking operation and to conserve the length of intestine torn away.

PORTAL THROMBOSIS occurred 21 times in 6050 autopsies as reported by Webster.[158] It was associated with

Cirrhosis of the liver	7 times
Carcinoma	6 "
Cholangitis	4 "
Amyloid disease	1 "
Ulcer of the Stomach	1 "
Banti's disease	1 "
As a primary phlebitis	1 "

Chalier and Longy[161] have encountered 4 cases of OBLITERATION OF THE INFERIOR VENA CAVA in ten years. If the process is slow and of

gradual development, a collateral circulation becomes established and wards off any danger; otherwise death is inevitable. Thrombosis, compression by tumor or other mass, and involvement in a malignant disease are the usual causes. The main symptoms are edema and the evidences of complementary circulation; as the latter develops, the edema subsides in some cases, but persists in others. The lesion is not necessarily fatal.

The Intra-abdominal Lymph Nodes.[162—164] A communication of Struthers,[162] giving his experience in regard to cases of ABDOMINAL LYMPHADENITIS resembling appendicitis in its clinical manifestations confirms that of Wilensky reported and reviewed last year in PROGRESSIVE MEDICINE. Cases are recorded by Struthers which show that an inflammatory reaction is present in the enlarged mesenteric glands. The enlargement was usually, but not always, due to a tuberculous infection. The symptoms closely resembled that of appendicitis. The cause of the reaction is an exacerbation of an old infection, an invasion with a fresh pyogenic infection (i. e., the onset of a mixed infection in a tuberculous node), or the occurrence of a transient adenitis similar to that seen in other parts of the body in association with surface infections. From the evidence submitted, Struthers is inclined to think that most of the cases are probably due to a reaction provoked by an extension of a tuberculous process.

I pointed out last year that the affection is a common one and should always be borne in mind in examining young patients presenting signs suggestive of appendicitis.

A somewhat similar corroboration appears in the German literature in the communication of Hollenbach;[163] his reports dealt only with tuberculous cases. Melman[164] reports a case of abdominal adenitis complicating a typical case of influenzal infection.

The Mesentery.[165—171] Valente[165] reports 24 cases of MESENTERIC CYSTS in children under seven years of age. The symptomatology is vague and indefinite until a tumor mass is discovered in the belly. When the cyst cannot be excised in toto, it is best to marsupialize it.

In adults the diagnosis of cysts of the mesentery is difficult because objective signs are wanting; and in cysts of the mesocolon it is probable that seldom, if ever, has a diagnosis been made before the abdomen was opened. The only clinical indication being an enlargement of the abdomen, unless this is discovered accidentally by the patient or found by the examining physician, the subject is not seen until some acute emergency demands immediate attention.

The cysts are distinguished from pancreatic cysts by their transverse mobility. These cysts must be distinguished from many intra-abdominal growths, particularly ovarian cysts, renal tumors, hydronephroses, pancreatic cysts, as well as from acute inflammatory processes. In addition, cysts of a similar structure may develop in the folds of the peritoneum—in the meso-appendix or gastro-hepatic omentum. Differentiation is, therefore, impossible from the very nature of things.

The cysts are divided into a serous and hydatid variety. The latter are rare. The serous cysts are due to some change in the lymphatic

system. Three hypotheses have been put forward to explain them, namely, degeneration of the lymph nodes, ectasis of the lymphatic or chyliferous canals, and rupture of lymphatic vessesl with encystment of the escaped fluids.

Since the appearance of the papers of Bigelow and Forman, and of Judd and McKay, reviewed last year, Ransohoff and Friedlander[168] have collected 15 additional cases of SOLID TUMORS OF THE MESEN-TERY.[166-168] Arising from the connective tissue within the mesenteric leaves, the tumors are invariably of the connective-tissue type of growth —fibroma, fibromyoma, lipoma and sarcoma. The primary retroperi-toneal sarcomata which grow between, and push apart, the leaves of the mesentery must be clinically and pathologically differentiated from the primary mesenteric sarcoma. Pathologically, the latter are nearly always fibro-, or spindle-cell, while the former which invade secondarily the mesentery are, as a rule, small or large round-cell tumors.

The x-ray findings are of diagnostic importance, except in tumors springing from the mesentery of the small intestine, since this latter have no definite anatomic nor x-ray location. The large intestine, both from an anatomic and x-ray standpoint, has a well-defined position and any gross variations are easily detected, even in the absence of obstruc-tion.

An important question which can only be settled during the operation is that of intestinal resection. If there is doubt of the viability of the bowel, resection must necessarily be practised, even if it enlarge some-what the operative mortality. The tumors are usually so closely connected with the bowel, and with the latter's blood supply, that there is always great danger of interfering with the bowel's nutrition in remov-ing the tumor.

In examining the reported cases, there is a striking similarity in certain salient points. The diagnosis is rarely made. The mortality in the operated cases is extremely high.

SURGERY OF THE STOMACH.[172-313]

Foreign Bodies in the Stomach[172-173] are found in three classes of persons: (1) In those who swallow objects accidentally; (2) in insane in-dividuals; (3) in mountebanks who swallow objects as part of their profes-sion. The articles that are swallowed are of a various nature and include smooth and round objects, or sharp and jagged things, such as needles or pins. Any of these may become lodged in the esophagus. If they descend into the stomach or intestine, they may lacerate or perforate the walls of the alimentary canal, or, passing safely onward, are extruded from the anus with the motions of the bowel. Multiple objects are sometimes swallowed. Practically all the latter cases come sooner or later to operation. The removal of foreign bodies from the stomach is a comparatively safe procedure. Jackson and Spencer[173] have been able to remove foreign bodies perorally through the gastroscope.

Havlicek[174] uses fascial transplants to reconstruct the hepato-gastric ligament in *gastropexy*. The motility of the viscus is said not to be

impaired by adhesions thereafter; and, whereas in the other methods
the new supporting bands show the tendency to strength, in Havlicek's
method they show the opposite tendency to contract.

Souligoux and Bloch[175-176] describe a new technic for *gastrostomy*,
which, they say, assures an absolutely continent opening. The stomach
wall is lifted up about 5 cm. high with three forceps, forming a cone, and
the tip of the latter is twisted exactly one-quarter of a revolution. The
walls of the cone thus fall into two or three spiral folds and these folds
are held in place with a few interrupted silk serosa sutures. A suture
is then passed entirely through the wall of the cone at the opening in the
tip of this thread, is then passed through the serosa and muscle of the
cone at its base. Four such interrupted sutures are taken around the
edge of the opening and each is drawn up and tied. The whole inter-
mediate part of the wall thus loops down inside and the resulting loose
invagination forms a most efficient valve to prevent egress of the
contents of the stomach while not impeding in the least the entrance of
any fluid.

D'Agostino's[176] method consists of dragging a cone of stomach wall
through a strip of rectus muscle. The contraction of the muscle is
supposed to exert a sphincteric action.

Pyloric Stenosis.[180-187] I went over the subject of pyloric stenosis in
infancy from the American point of view last year. There can be no
doubt as to the need for surgery in the average case of hypertrophic
pyloric stenosis in accordance with the principles I reviewed last year.
The whole question, insofar as it concerns the need of operation in a
given instance, hinges not on the size of the tumor, but on the complete-
ness of the pyloric obstruction and the consequent interference with
absorption and growth. English experience, according to MacDonald's
report, coincides with our own that early surgical treatment is indicated
in all cases. He agrees that Rammstedt's operation appears to be the
best procedure. The report of Squarti,[180] from Italian sources, appears
to favor surgical therapy also and the Rammstedt operation. Conti-
nental experience in Germany and France, as shown by the papers of
Pehu[183] (French) and von Bokay[184] (German), differ from the American
and English viewpoint. Twenty-six cases have been published in the
French literature; and, according to Pehu,[183] the experience is that even
in bad cases a cure may be obtained under persevering medical measures
alone. Von Bokay,[184] also advocates medical treatment, an essential
part of which is the systematic subcutaneous injection of papaverin
hydrochloride. I do not know how much of the latter's opinion is
influenced or determined by the fact that a large proportion of his cases
were due to spasm alone; but he had 8 cases, in which the pylorus could
be palpated as a hard cylinder, which made a systematic recovery under
this form of medical treatment. In one of these, a recurrence of the
trouble was controlled by a second course of papaverine injections.

Ramsay's[185] (English) mortality for the Rammstedt operation is
rather large. The best American statistics put the figure at about 20
per cent. Ramsay's figure was 50 per cent.

The *end-results of this operation* were investigated by Pannett.[186]

The operation leads to a certain increase in the immediate evacuation time of the stomach, but the latter may, or may not, be a temporary phenomena. Whether unoperated patients are later handicapped by the abnormal pylorus has not yet been settled.

Pylorospasm. Pylorospasm is observed with comparative frequency. It may exist in various types: the neurotic, the irritative and the reflex. As a pure neurosis pylorospasm is rather uncommon, occurring, according to the experience of Finney and Friedenwald,[188] in but a small proportion of all gastric affections. The purely neurotic form occurs more frequently in females. In a large percentage of the cases, pylorospasm is secondary to some gastric or abdominal lesion, as gastric or duodenal ulcer, cancer of the stomach, enteroptosis, gall-bladder disease, etc.

The symptoms of pylorospasm vary in intensity according to the degree of the spasm; they are rather characteristic. They consist of pains of the hunger type appearing two or three hours after meals, which are relieved by emptying the stomach of its contents as well as by the ingestion of food, and of contractions of the stomach leading to pseudo-tumor formation. At first the spasm appears periodically, later it persists, with consequent obstruction and retention of food. Under these conditions the stomach content presents all of the characteristics ordinarily seen in cases of pyloric stenosis. Constipation and emaciation are late symptoms. The physical examination shows tenderness, and, in thin patients, a definite mass can be palpated in the pyloric region which has the property of becoming less distinct as the spasm relaxes. There is usually present a hyperacidity, or hypersecretion, the degree of which depends largely upon the duration of the symptoms. Roentgenologically, it is possible to differentiate between the functional and organic cases.

An important element in the treatment is the correction of the primary disorder, whether functional or organic. In certain cases an ulcer cure with the patient in bed has given Finney and Friedenwald satisfactory results. For the intractable cases which resist all forms of medical therapy Finney and Friedenwald recommend pyloroplasty. Their experience in this regard corresponds to that of Rogers.

For cases of OBSTINATE HYPERCHLORHYDRIA, Babcock[189] suggests the operation of *cholecystgastrostomy*. In an experience of 27 cholecystgastrostomies and 17 cholecystoduodenostomies Babcock noted no ill effects. He goes so far even as to recommend these operations for ulcer. For practical purposes this operation reproduces the consequences of a gastroenterostomy, at least insofar as the introduction of duodenal contents into the stomach is concerned.

I have no personal experience with this operation as a curative measure in the two conditions for which Babcock recommends it. However, I do know of two significant facts: (1) Ulcers flourish in the wall of the duodenum; and (2) the introduction of the alkaline juices usually has but a temporary effect. I investigated this latter question several years ago, and was able to show that within a certain time after operation —usually not a very long time—the *status quo ante* becomes reëstablished and sometimes becomes aggravated.

Gastric and Duodenal Ulcer.[190-257] For practical purposes chronic ulcers of the stomach or duodenum conform themselves to one of two types: The first of these—and, perhaps, the less important—are the soft lesions characterized (1) by their relatively smaller size, (2) by their superficial extent, (3) by the failure of the process to penetrate any deeper than the submucosa, (4) by the absence of surrounding areas of induration; noted (5) by the frequently greater benignity of the clinical course, (6) by the tendency not to undergo malignant degeneration, (7) by the frequency with which cures are obtained by medical means alone.

The second group contains the lesions characterized by (1) their comparatively larger size, by their deep penetration and frequent perforation, (2) by their marked induration and by their numerous and dense adhesions to surrounding organs, (3) by their marked chronicity and frequent "relapses;" noted (4) by the frequency with which malignant changes are found throughout the lesions or limited to its bed or margin, (5) by the tendency to complications of a mechanical nature accompanying their progression. There are cases in which the characteristics of the one overlap into that of the other, or in which a proper distinguishment of the lesion is made difficult or impossible because of many associated phenomena frequently of a functional nature. (Wilensky.[194])

The old conception that a typical history indicates absolutely the presence of an ulcerating lesion seems to have been generally abandoned. It is quite true that many times the operative exploration fails to reveal the presence of any ulcer; but it is equally true that just as often a rather indefinite or trivial history is proved to be due to very large lesions in the wall of the stomach or duodenum. Experimentally, it is rather well known that defects in these organs can be produced in very many different ways and repeatedly in the same animal, and that all of these artificially-made lesions have the marked characteristic of healing promptly and rapidly. It does not seem unreasonable to assume that in human pathology there are numerous occasions when temporary defects of a relatively similar origin and nature appear in the stomach wall and that these too would heal quickly. Unless these were looked for fairly promptly, the likelihood is very strong that they could not be demonstrable. Yet such lesions would give symptoms; and there is no reason why these should not be as typical as any described. It is conceivable, therefore, that the original viewpoint of Moynihan, and others, may have some basis of truth; namely, that a typical history always spells an ulcerating lesion, with the distinct proviso, however, that a great many of these undergo rapid and spontaneous healing. If placed under treatment, recovery would follow, with complete disappearance of the symptoms, and the effect might be a permanent one. I am quite sure that many of the "medical ulcers" are of this type. If, for any reason, new ulcers developed subsequently, the symptoms would reappear again, and, as healing again took place, these would disappear once more. A great many of the remissions seem to be explainable upon this basis. (Wilensky.[194])

A number of known facts were reiterated and emphasized in the

discussion at the New York State meeting[195-199] this year. Of 100 people with gastric distress, 20 are due to organic disease, 40 have disease remote from the stomach, 40 have disease outside of the abdomen. There are many reflex causes for stomach complaints; disease of the female generative organs, disease of the central nervous system, toxemia, tuberculosis, syphilis, cardiovascular disease, etc.

History taking is an art; the interpretation of a history is a science; success accompanies and corresponds to the ability to pick out the relevant from the irrelevant. Most of the discussion went to show that there has been no substantial advance in the ability to diagnose ulcer. Except in those fortunate cases in which there are positive *x*-ray evidences (*i. e.*, niche of Haudek) the criteria employed are of an indirect and circumstantial nature. I do not speak of the accidents of hemorrhage or perforation, but of the average case of ulcer. In those without definite proof of a stomach defect the operation degenerates into an exploratory laparotomy. To be sure, as one acquires a larger and larger experience, one attains the "knack" of being able to distinguish the chaff from the wheat, an ability which is not based on a sound foundation, but which, in a large majority nevertheless, becomes a valuable aid. It is very significant that in Kocher's[200] cases the diagnosis of florid ulcer was correct in only 86 per cent. In the majority, the manifestations of ulcer form only part of a general pathologic condition.

The rational treatment of ulcer is a very difficult matter and should be determined for the most part upon the anatomic characteristics of the lesion present. When the evidence is essentially indirect and more or less of a presumptive nature, there is room for differences of opinion. When the evidence, however, is direct and conclusive, there is only one rational course to pursue; these latter lesions are those which can be definitely demonstrated as perceptible defects in the roentgenographic examinations.[194]

I heartily agree with C. H. Mayo[201] that the medical treatment of ulcer is the treatment of the exacerbations and is directed toward lowering and controlling the gastric acidity by dilution and neutralization of the gastric contents at regular periods. Generally this, however, does not lead to a permanent cure. The procedure is carried out while the symptoms are acute. Patients are under surveillance for a long period, with repeated tests of stomach function and upon a regulated diet. Such treatment, effective as it is in affording relief of symptoms, can seldom be obtained by the majority of those afflicted; the patients are too poor; or for other reasons, equally potent, this method of therapy is not securable. While freedom from symptoms following an exacerbation does not necessarily mean that the lesion is healed, it must be said that the relief of symptoms gives satisfaction to a certain group of patients. Naturally, there are certain dangers when such medical courses of treatment become repeated, the danger of malignant transformation is, however, not nearly so great as the dangers of hemorrhage and perforation.

Judging from the many and varied reports in the literature, it would seem that there is a wide divergence of opinion between medical and

surgical men with regard to the results of treatment. Most of this divergence of opinion disappears, however, when the various viewpoints are correlated and properly integrated with one another. The internist, in urging medical care, refers to the dangers of surgery and to the bad results which so frequently follow operation. The surgeon refers to the frequent recurrences after medical treatment, to the dangers of hemorrhage and perforation, to the liability to cancerous degeneration. The one refers to indications which are readily agreed to by the internist; the other to deficiencies of therapy which are visible to everyone and which are more and more being recognized by the surgeon. If we keep our viewpoints alike and stick to the subject in hand, namely, ulcer, *i. e.*, an actual lesion and not symptoms which can mimic those of ulcer, everyone agrees fairly well. Differences of opinion of this kind can only lead to the just consideration of the advantages and disadvantages of the medical and surgical parts of the problem; for, as I have pointed out previously, the treatment of gastric and duodenal ulcer is a complex matter requiring the combined knowledge of both the internist and surgeon in which either the medical or the surgical elements must be considered as component incidental factors in the total picture.

What are the possibilities for the spontaneous healing of a stomach ulcer? Some ulcers, at least, must heal; for, otherwise, there would be no cicatricial pyloric stenosis, nor hour-glass contractions without open ulcerating defects.[252] Ivy studied the healing-time of gastric defects in animals. Normally the healing-time of an acute ulcer, from one to one and a half inches in diameter in the mucosa of the antrum, varies from twelve to eighteen days. The healing-time of a defect in an exposed pouch of the stomach varies from fifteen to twenty days. When these defects are manipulated several times daily until congestion and bleeding occurs, the healing-time varies from thirty-four to fifty days and the scar formation is very marked. The delay is similar to that caused by partial pyloric stenosis in acute experimental ulcer. The manipulations—which would correspond to irritation by ingested food and congestion incident to the digestive period—delay the proliferation of the mucosal cells at the edge of the ulcer and prevent them from getting a foothold on the base. In other experiments, injections of pus and bacteria were made into the ulcerating area in addition to the manipulations. The healing-time varied, under these conditions, from thirty-three to forty-three days, a fact which showed that the healing was not appreciably delayed by infection. These experiments corroborate the findings of Wilensky and Geist[551] made some years ago incidental to an attempt to prevent the healing of acute defects by the injection of streptococci into their bases; the healing-time of the defects was within the limits found by Ivy.

The possibilities of healing under conservative forms of treatment are demonstrated clinically by Buckstein[206] with the aid of roentgenographic evidence. The special objective of the investigation was to demonstrate the effectiveness of the principle of rest as applied in the treatment of gastric ulcer. The patient had a large lesion on the lesser curvature. Two facts appear to be clearly demonstrated: (1) The

gradual healing of the defect; and (2) the improvement in the emptying-time of the stomach. Unfortunately, there is no extensive investigation in the literature along these lines which could give us a mathematical conception of the frequency with which this occurs. An investigation of this kind is highly desirable.

The very fact that healing has been demonstrated, both experimentally and clinically, is a very significant fact, one which must necessarily lead us to give this advantage to every one suffering with an ulcer even if the latter have all the earmarks of a lesion which, ordinarily, one is accustomed to regard as being beyond the pale of medical and conservative forms of treatment. I have no doubt that many patients with well-defined ulcer undergo a spontaneous cure; not all of us consult the doctor with our complaints; nor do all doctors—even the best of us—always recognize the presence of this lesion.

The general opinion, however, that the great majority of ulcers can be cured by conservative means alone and can be kept cured under proper after-treatment is susceptible of modification and is properly applicable to the soft ulcers. The further opinion that most medical men push the matter of medical therapy too far, and that an ulcer persisting after proper medical care becomes a surgical malady, is one which necessarily must also be modified in view of the newer knowledge. I believe that when there are no complicating factors present in addition to the general and ordinary manifestations of ulcer—especially no retardation of the emptying-power of the stomach—medical treatment is preferable. When stasis of the stomach is well established, in an uncomplicated ulcer, then surgery is indicated.[194]

The question of operation arises from a number of different viewpoints and causes. From the viewpoint of the ulcer itself, the causes can be classified as being (1) due to the symptoms of the ulcer itself, (2) to the consequences of the lesions, (3) to its accidents, and, (4) to the danger of malignancy.

1. The advisability of operation is still doubtful in simple ulcer uncomplicated in any way. In some cases the pain of ulcer is a pronounced factor and, when the symptom is intolerable and intractable, operation must be thought of. In other cases the fairly frequent recurrence of symptoms demands such a large portion of the patient's time under medical care either at home or in the hospital, as to make the time-saving factor of operation worthy of some consideration. Similar lines of thought are to be considered for business reasons; or by one about to depart upon a journey to places where expert aid is not available should any of the accidents of ulcer occur.

To be sure, the number of cases to be operated upon for such reasons must be comparatively few. For all of these the pros and cons ought to be carefully weighed. The important point to be remembered, and one which cannot often enough be emphasized, is that in such cases operation of any kind is only an incident in a much larger, carefully-prepared program; for it is in just this class of case that the largest number of failures can be credited to surgical therapy alone.

2. Operation is much more frequently indicated for the consequences

of the ulceration. The most important of these are those which disturb the motor activity of the stomach, either by paralyzing the latter by its mere presence, or by causing a spasm of the pylorus, or by both of these acting together. I agree with Schuller on this point that disturbances of the motor activity of the stomach are one of the important indications for operation in cases of ulcer.

The other broad group of cases in this category include those which result from the attempted or consummated healing of the lesion—to pyloric stenosis, or to cicatricial deformity of the body of the stomach. Operation, in these cases, is a necessity. Almost universally, it is agreed that the best results of surgical therapy are obtained in this general class of case, and the most important reason for this is that surgery supplies something which Nature cannot do for itself, it remedies a mechanical and structural defect.

3. Operation is an urgent necessity when the accident of perforation happens to an ulcer. There is no question here of the necessity of operation; the only question to be discussed is the matter of technic and procedure. These will be discussed later. Operation may, or may not, be an urgent necessity in the matter of the accident of hemorrhage; this question, too, I purpose discussing later.

4. The danger of malignancy makes another strong indication for operation. Opinions vary as to the frequency of this change, but, whatever the percentage or etiologic relationship, the fact remains that approximately 20 per cent of such gastric lesions—and I speak here especially of the large, penetrating lesions—have carcinomatous tissue within their structure. On other occasions I have pointed out the importance of this fact as an indication to regard every one of such lesions as potentially malignant.

The question of operation for gastric or duodenal ulcer must also be considered from other viewpoints. Other things being equal, C. H. Mayo[201] points out that the indication for operation should be more definite in cases of ulcer of the lesser curvature than in cases of pyloric or duodenal ulcer. He mentions, however, one disturbing factor: Hunter, studying the material at the Mayo Clinic, found that the average death-rate for the four-year period after operation in patients with gastric ulcer was slightly more than three times the normal, while in patients with duodenal ulcers it was, if anything, slightly less than normal.

Other things being equal, operation would receive more consideration when the patient's condition and resistance powers are good, and especially when there is little evidence of hepatic or renal insufficiency, or of cardiovascular disease. When, in this latter class of patients with deterioration of the vital functions, operation becomes a necessity, that type of operation should be chosen which is least conducive to an unrecoverable operative insult.

As to the best surgical method of therapy, excision remains the operation of choice. It cannot always be the feasible method, much depending upon the location of the lesion, its size, and other mechanical considerations. Destruction of the lesion seems most desirable and

necessary (1) to get rid of the lesion itself—a very obvious advantage; (2) to prevent the accidents of hemorrhage and perforation; and (3) to prevent malignancy. Both Deaver[209] and C. H. Mayo[201] agree that when the ulcer has not to any great extent impaired the motility of the stomach, simple excision suffices.

The most favorable ulcers for excision are those on the walls of the stomach and small ulcers on the lesser curvature. In excising these latter ulcers, it is best to close the wound in a direction opposite to that in which it is made. Deaver recommends for ulcers at the pylorus, the most common site of the lesion, pylorectomy. For a large number of these, however, I believe that pyloroplasty would be suitable. Large callous ulcers at the middle or to the left of the median line of the lesser curvature are best treated, according to Deaver,[209] by circular resection and end-to-end anastomosis with posterior gastro-enterostomy.

Ulcers on the posterior wall can usually be excised by making an opening in the anterior wall and dealing with the ulcer through the resulting wound. After closing the wound, the suture line on the posterior wall can be reinforced by entering the lesser space. An adherent ulcer is best approached above the stomach through the lesser cavity. In order to avoid reformation of adhesions in these latter cases, W. J. Mayo recommends, after closing the stomach wound, to bring up the great omentum through an opening in the gastrocolic omentum, carrying it up between the stomach and pancreas and fastening it over the suture line. Delgado[221] warns against pylorectomy or partial gastrectomy in this type of ulcer when the lesion is adherent and prefers some form of local resection.

In the treatment of duodenal ulcers, Deaver[209] acknowledges that one cannot be quite so free with radicalism, except in ulcers of the first portion. Roeder[207] recognizes three types of lesion in the duodenum. (1) The large ulcer with an abundance of scar-tissue formation which he thinks can be relieved perfectly by gastroenterostomy. (2) The medium-sized ulcer with too much scar-tissue to allow for primary resection. Gastro-enterostomy is evidently a doubtful procedure here. (3) The small ulcer, which is susceptible of being removed, is becoming the most frequent type, Roeder[207] thinks, and here he agrees with C. H. Mayo,[201] von Haberer[282] and Deaver[209] as to the possibilities of simple excision.

When excision of some form is not feasible, the surgeon is left with the choice of gastro-enterostomy or pyloroplasty. Clendenning[222] and C. H. Mayo[201] agree that gastro-enterostomy alone seems to be continually losing in favor.

I have gone over the status of gastro-enterostomy a number of times in previous numbers of PROGRESSIVE MEDICINE, and the status seems still unchanged. If we accept Paterson's view, referred to by C. H. Mayo,[201] that gastro-enterostomy continuously applies the principles of medical treatment—and there is no valid reason why one should not—there would be ample explanation for the profusion of recurrences after gastro-enterostomy alone. It is a confession of weakness for the operation when Clendenning says that, "On account of its simplicity

it is a good operation for the general surgeon." And if one analyzes the cases in which gastro-enterostomy gave good results in Clendenning's[222] experience, one finds that these are cases of pyloric stenosis.

Davis[232] compares the operations of gastro-enterostomy with pyloroplasty. As results now stand, from 15 to 40 per cent of the gastro-enterostomy cases are failures. At least they do not restore the patient to health. Davis[232] is willing to concede that many of the failures are avoidable, but even with these surgical errors eliminated, numerous cases report for treatment with symptoms little improved, or as bad, or worse than before the operation. The stubborn fact persists that there are many disappointing results, even when the operations are done by the best of surgeons. Moynihan agrees with this. Most of the symptoms are due inherently to the gastro-enterostomy. Although gastro-enterostomy has no doubt done an enormous amount of good in the past, I agree heartily with Davis[232] that there are reasons without number why a more physiological method should be adopted in the treatment of these cases.

In view of these discouraging facts relating to gastro-enterostomy, Davis[232] makes a strong defense of the operation of pyloroplasty. A number of men—Moynihan, Kocher, Warbasse, Binne—are quoted as being in favor of the Finney operation. Davis[232] is more than right in saying that, unfortunately, most of the surgeons who speak kindly of pyloroplasty go right on performing gastro-enterostomies. That more do not resort to some form of pyloroplasty is due to the fact that they are familiar with gastro-enterostomy and because of a widespread, but erroneous, opinion that the sufficient mobilization of the duodenum is extremely dangerous and difficult.

The two general types of pyloroplasty are the Heinecke-Mikulicz operation and the Finney operation. The former does not seem adequate as usually done. The Horsley operation appeals better to Davis.[232] The operation done by Finney seems to meet all requirements and the size of the opening may be made as large or as small as seems necessary in the individual case. Finney and Friedenwald advise dealing with the ulcer through the incision in the organ and consider "the opportunity thus afforded to explore digitally and inspect the ulcerated surface and then excise it through this incision is one of the strongest points in favor of the operation."

Pyloroplasty has the advantage of permitting the digestion to go on normally. The opening is the regular channel. Even when the sphincteric action is destroyed, segmentation of the duodenum will prevent the stomach from emptying too rapidly. Later, if the opening is not too large, the pyloric sphincter will function to a certain degree on the same principle that the anal sphincter acts after it has been cut.

The paper of Moore[233] confirms these viewpoints.

Abroad, opinion in regard to gastro-enterostomy seems divided. Moynihan[280] and v. Haberer[282] lean to the majority American opinion favoring excision. Kocher still favors gastro-enterostomy; Metraux[235] agrees with Kocher. I do not agree with many of the objections he raises as being beside the point, nor with his explanations. I am rather

astonished that in 210 cases of operated ulcer, he has come across no case of jejunal ulcer. In Pauchet's cases, as studied by Menghetti,[224] good results are claimed in 90 to 95 per cent of the cases. In view of this, it is surprising that Pauchet considers any other forms of operation. Gross'[237] experience agrees with that of Kocher, and Metraux[235] even with ulcer in the body of the stomach. Gross has a new operation which he calls enlarged excision, however. This includes cutting off the pylorus as the first step and slitting the lesser curvature lengthwise. A new outlet is then made which is rather large. The operation leaves the stomach shaped like a moccasin.

Brütt's[220] analysis of the material in Kummell's clinic at Hamburg indicates that, for ulcers away from the pylorus, they are preferring transverse resections of the stomach; the mortality is 5 per cent as against 4 per cent for gastro-enterostomy. Eiselsberg,[238] also, is following the present trend away from gastroenterostomy to more radical treatment of gastric and duodenal ulcer. His experience has converted him to the view that the Billroth II method is the preferable one for the present; however, he has recently been employing the Billroth I technic with good results. Recurrences have been observed with the Billroth II operation, but, mostly in the form of peptic ulcer in the jejunum. If time proves that recurrences are common with this method, Eiselsberg believes that he will return to the gastro-enterostomy. In doing the Billroth II operation, Toupet[239] prefers doing an antecolic posterior gastro-enterostomy. With this technic the colon is not brought to the surface and in difficult cases it permits operating outside of the abdomen.

A comparison of the Billroth I and II operations with transverse resections is made by Suermondt[240] from the material at the Leyden clinic. The data consists of x-ray observations and test-meals. The outcome in the Billroth II operation seems incomparably better; the stomach empties itself more rapidly and more completely than with the other methods, and all the patients have gained weight. As the food escapes more quickly, there seems to be less tendency to hyperchlorhydria. Kloiber[241] explains the decreased acidity on the ground that the removal of the antral segment of the stomach results in a decrease of acid-producing membrane. I am not sure, however, just how much this explanation is worth because the bulk of the acid is produced in the cardiac end of the stomach, and, on the basis of compensatory effort, the deficiency ought to be easily corrected. The observations of Ivy and Oyama[242] bear this out. However, clinically, the resection operations seem to diminish the hyperchlorhydria, and for that reason they are preferred by Stierlin, Kelling[275] and von Haberer.[280-282]

For duodenal ulcers, Schmidt prefers resection of the ulcer-bearing area whenever it is technically possible. Von Haberer has quite a series of cases of duodenal ulcer resection in which he has good results.

Kleinschmidt[243] reports 76 cases of transverse resection of the stomach. Twelve of the patients died—a rather large mortality. In Eiselsberg's[238] last series of 99 similar resections, the mortality was 2 per cent. The immediate results of this operation are very good. In a series of 64 cases which Eiselsberg operated before 1918, the ulceration recurred in

9, and a new operation was required in 4 of the patients. In Lecene's[246] cases—5 in number—done from seven to eleven years ago, the present contour of the stomach, as shown roentgenographically, is practically normal. I am especially interested in the roentgenologic report of Lecene. In the experience at the hospital to which the reviewer is attached, the usual thing to be expected is a deformity of the body of the stomach which, to all intents and purposes, closely resembles that of the hour-glass type. The interesting thing, however, is that this is a good type of operation in spite of the stomach deformity, and that it yields good clinical results.

I am interested also in the number of recurrences of ulcer reported in Eiselsberg's[238] earlier series. These new ulcers have a habit of recurring almost exactly at the site of the original defect which is practically always represented by the suture line. It is a question of importance whether these are reimplantations of the original ulcer cause in the suture line and whether they have not close relationships with the so-called gastro-jejunal ulcers.

In Kummel's[245] series of 862 cases, 1.62 per cent were on the greater curvature. According to Timbal,[247] the prognosis of this type of ulcer is not so favorable. Localized peritonitis forms in the lesser sac, and there is a great tendency to hour-glass deformation of the stomach. Ulcers of the greater curvature are least amenable to medical measures, and surgery should be resorted to early.

In summing up the entire situation with regard to the therapeutics of ulcer, one must agree with Eusterman[257] that the change from the nihilism to a rational attitude augurs well for the patient with ulcer. "Medical treatment has been discredited not because the principle is wrong, but because the effort was inadequate, and the coöperation of the patient was not sufficiently cultivated. Consistent medical management is often superior to poor surgery. The prospect for cure following a successful operation has too frequently been forfeited through gross indiscretions. . . . All of this emphasizes the necessity of friendly coöperation between the internist and the surgeon." Unquestionably, the best interests of the patient are met by this requirement; one which I have spoken about previously in PROGRESSIVE MEDICINE and elsewhere. "It seems safe to predict that the pooling of all therapeutic resources will prevail over the present tendency of surgeons to institute newer and more radical measures in surgical technic for the cure or alleviation of a widely prevalent and increasing disease."

In studying a series of 151 cases of HOUR-GLASS CONTRACTURE OF THE STOMACH[258–262] Holland[258] found that 128 of them occurred in women. Only 8 of the cases in men followed simple ulcer; the others resulted from a carcinomatous growth, or followed an injury or an old gastroenterostomy operation. Segmental resection of the constricted part of the stomach is evidently the operation of choice as it makes possible the removal of the lesion and the reëstablishment of the continuity of the stomach. This type of operation is, however, not always practicable; it is dangerous, for instance, when a cicatricial ulcer is intimately fixed to the pancreas and when the patient is markedly anemic. For such

difficult cases, Lecene prefers gastrogastrostomy done according to the Finney technic. This procedure leaves the ulcer *in situ* but makes possible the formation of a large anastomotic opening between the two gastric pockets. Lecene[246] does not, however, add that it would enable one to deal locally with the ulcer (cauterization, etc.) while the stomach is open. The end-results of gastrogastrostomy are not as good as those of segmental resection; the ulcer may heal, but, even if it does, trouble persists.

In cases of close fibrous mesogastric stenosis, a gastro-enterostomy on the cardiac side of the contracture, or even in both pockets, is much less physiologic than a gastrogastrostomy and the results are poor. For that reason, Lecene[246] does only mesogastric resection or gastro-gastrostomy. Goullioud resects the entire pyloric pocket ("hemi-gastrectomy"); other cases in which this operation was done have been reported by Berard and Budinger (1899). Goullioud[259] advises doing the operation in two stages; first, the gastro-enterostomy; second, the resection. In 1904, Santy collected the reports of 20 cases treated by hemigastrectomy, and 44 cases treated by mediogastric resection; the mortality of the former group was 20 per cent, while that of the latter was 13.6 per cent. The late clinical end-results of the hemigastrectomy were most satisfactory.

At the Mayo Clinic, the general operative mortality of hour-glass stomach is 7.4 per cent. Sleeve, or segmental, resection is the operation of choice. If the condition recurs, the lower half of the stomach is removed at a second sitting using the Polya technic.[286]

PERFORATED ULCER.[263-273] *Penetration* of the lesion *through the base of an old established ulcer* and when the nourishment of the patient is at par results from the gradual progression of the pathologic process and is invariably accompanied by protecting adhesions around the lesion on the peritoneal side of the stomach wall which effectually lead to a safe walling off of the base of the ulcer and to the prevention of any sudden outpouring of gastric contents into the free peritoneal cavity. A *sudden perforation* into the free peritoneal cavity through the base of an old ulcer under the conditions just described is indicative of a lack of healing-power on the part of the individual. The mechanism in some of the cases of this kind may, however, be independent of the healing-power and is similar to that which causes the occurrence of acute per-forations in the absence of any preëxisting lesion. Here it assumes the characteristics of an embolic phenomenon occurring during the course of some temporary bacteremia, the evidence of which may be so tran-sitory as to be undemonstrable. There is much evidence in the fields of experimental, and in that of clinical, medicine which makes these assumptions highly probable. (Wilensky.[194])

All success in the treatment of this lesion is based on early treatment and upon the efficient closing of the opening. Successes are occasionally reported by such other means as tamponade, or drainage to the ulcer site, etc., but in no sense do these rival the direct closure. Concerning simultaneous gastro-enterostomy in the immediate treatment, there is as yet no general agreement. The arguments pro and con have

become very familiar to most of us, and are largely theoretical. The figures of Deaver,[263] and of other man—Schulein,[265] Straule,[264] Lewisohn,[268] Basset and Uhlrich,[266] etc.—show that there is no discrepancy in immediate results that could be attributed to the performance or non-performance of the primary gastro-enterostomy.

Leaving out of consideration those cases in whom the precarious nature of conditions make gastro-enterostomy inadvisable, it seems to me that the question of the addition of the latter operation should be decided upon the merits of gastro-enterostomy itself. The argument advanced by Deaver that "it has been abundantly demonstrated that it is successful in such a high percentage of cases that there is no longer any doubt of its specific effect," is one which will not be concurred in by a very large number of men, and one which everyday experience does not uphold. Under such conditions it would not be wise to do gastro-enterostomy as a primary measure. For, in the first place, in a certain number the perforation being an embolic phenomenon will not be followed by any sequelæ at all; and, in the second, it would be much more sensible to await an interval free from the dangers of an emergency, in which the question of further operation could be weighed and measured and a proper course of action could be determined upon based on the newer conceptions of the proper therapy of ulcer in which gastro-enterostomy is distinctly an operation of second or third choice.

A case in which gastric perforation recurred five times in the same patient is reported by Henry.[273]

GASTRIC AND DUODENAL HEMORRHAGE.[274–275] Finsterer[274] is convinced that the percentage of fatal hemorrhages from ulcer of the stomach or duodenum is larger than is supposed. With a large erosion, spontaneous stoppage is scarcely possible, so that the danger of waiting surpasses those of intervention. Finisterer therefore prefers operation. Kelling's[275] experience is that the mortality of hemorrhage is about 12 per cent; he recommends, a number of conservative measures before resorting to operation. When operation is indicated, resection of the ulcer is the procedure of choice.

Postoperative Peptic (Gastrojejunal or Jejunal) Ulcer.[277–288] Mandl's[278] survey of the German literature shows that there are over 200 cases recorded. The number of cases in the literature seem to be constantly growing. The symptoms of gastrojejunal ulcer are so continuous, or the recurrence of attacks so frequent after some months of apparent cure, and they consult so many physicians, that C. H. Mayo[201] believes that each single case apparently stands for a multitude of failures.

The spontaneous cure of one of these postoperative ulcers is of very rare occurrence. The cause of ulcer of the jejunum is intimately connected with the operation of gastro-enterostomy. Doubtless many ulcers after gastro-enterostomy do not come to operation, and for every ulcer there are cases of irritation of the stroma or of hyperemia or frank inflammation. von Haberer[280–282] goes right to the very root of the subject: in the last analysis it may be said that patients with this lesion have a "predisposition" to its formation in which the other factors—the chemical composition of the gastric juice, the vascular changes, and

the nervous changes—probably play only a part. Postoperative peptic ulcer, in von Haberer's experience, has depended quite materially on the type of operation employed for the original ulcer. After resection operations, the secondary ulcers occur very rarely. A very significant fact which von Haberer brings out is that, in 71 cases in which a unilateral pyloric occlusion had been practised, the secondary ulcers appeared 14 times; this is, comparatively, a very large percentage.

The problem of gastrojejunal or jejunal ulcer is very important. The various factors about which much is said—clamps, sutures, trauma, etc., —as etiological causes must play an insignificant role, otherwise the number of cases of secondary ulcer would far exceed the 2 or 3 per cent of all gastro-enterostomies which are being done. If one carefully examine all of the available information, one cannot help the conviction that gastrojejunal or jejunal ulcers could be entirely eradicated if one would give up entirely doing gastro-enterostomy (Wilensky).[194] This is probably the reason for the reversion of von Haberer to the principle of the Billroth I operation. He presents a long array of arguments in favor of this operation as a prophylactic measure against the secondary ulcerations and he is confirmed in this viewpoint by the experience of Denk.[283] In the same spirit, Horsley[279] speaks of pyloroplastic operations. Evidently, the tendency to avoid gastro-enterostomy is growing.

As regards *treatment*, conservative measures are usually inefficacious in the experience of the Mayo Clinic, as given by Judd.[286] The Mayo plan of procedure is to undo the gastro-enterostomy, excise the secondary ulcer and then to close the openings in both the stomach and intestine. If the original ulcer is also still present, the latter is excised. At the same time, a plastic operation is done at the pyloric outlet if it seem advisable. A new gastro-enterostomy is avoided as much as possible because more ulcers form in spite of all precautions.

In case a fistula has formed between stomach and colon, or between colon and small intestine, the operation is very difficult. A large tumor is generally present, made up of adherent, thickened and edematous coils of intestine and omentum. When a cleavage plane can be found, it may be feasible to expose the anastomosis, separate the parts and close the opening. Whenever possible, this should be done in preference to resection which is a very formidable procedure. So formidable is the operation in some cases as to make it advisable to do a jejunostomy below the tumefaction for side-tracking and feeding purposes. This is the technic employed at Mount Sinai Hospital as reported by Lewisohn;[277] under these conditions the jejunostomy causes a disappearance of the tumefaction and a symptomatic cure of the secondary peptic ulcer and its complicating factors. In one case detailed by Lewisohn,[277] it was possible at a subsequent operation to demonstrate that the ulcer had healed anatomically.

Linitis Plastica.[293-294] One of the difficulties of medicine is illustrated by the number of synonyms which Palmer[293] has collected for linitis plastica; it is perfectly ridiculous to have a dozen different names for a single pathologic entity.

Linitis plastica was first studied by Andral, in 1854. It is a disease

affecting the stomach and, very rarely, the small and large intestine, from which it spreads to the adjacent structures. The essential lesion is a diffuse and marked hypertrophy of the submucous connective tissue, and, to a less degree, of all of the coats of the stomach or intestinal wall except the mucosa where there occurs an atrophy of the glandular elements. The stomach walls become markedly thickened to six or eight times their normal, and are rigid and hard like a leather bag. There are two forms of the disease, the localized and the diffuse. The localized is usually situated at, or near, the pylorus; the diffuse extends from this region toward the cardia and may involve the entire stomach. The lesion never involves the duodenum.

The chief characteristic of the affection is a slow, progressive stenosis of the stomach, leading to food stagnation. The onset is gradual, and the symptoms include loss of appetite, disturbed digestion, eructations of gas, vomiting, loss of weight, and cachexia. The symptoms gradually increase in severity; finally, complete stenosis results, producing death by starvation.

Carman characterizes the roentgenologic characteristics as being those of a filling-defect with a relatively smooth inner margin and with peristalsis absent from the involved area. LeWald is more cautious in his descriptions.

The disease is amenable to surgical measures only, and gastrectomy is the operation of choice. If the condition of the patient is impaired—and this is very frequently so—the operation should be done in two stages.

Linitis plastica resembles scirrhous carcinoma and cirrhotic syphilis of the stomach. The major part of the histologic change would seem to be a sclerosing process. The question of malignancy has been widely discussed and the matter is confused by a tendency to describe both benign and malignant types. Ewing believes that all of the cases are probably atypical cases of sclerosing fibrocarcinomata; lymph node or distant metastases, however, seldom occur. Harrigan describes it as essentially a benign form of fibrosis.

One case is reported this year by Enriquez and Gaston-Durand[294] in which a spontaneous retrogression of this lesion occurred. In spite of the fact that a course of antisyphilitic treatment had at first been ineffectual, I feel sure that syphilis played a very important role.

Carcinoma of the Stomach.[297-307]   The exact starting point of carcinoma of the stomach is unknown, but the earliest cases of cancer have been observed on the edges of indurated ulcers. Kraske[298] again reflects the generally-held German opinion that this latter change is extremely rare. That this change can take place has been known for a long time, but the frequency of its occurrence has been overestimated. The various men who have studied this phase of the problem—Mayo Clinic group, Ewing, Wilensky and Thalhimer, and now von Bomhard—have come to quite different conclusions. In general, von Bomhard concludes that the malignant transformation is relatively rare. According to Konjetzny, we may assume that a cancer has developed on an ulcer basis when the ulcer shows the gross characteristics of a benign lesion

throughout its structure and a partial cancerous infiltration. (Even this is not an absolute criterion. Reviewer.) The difficulties of distinguishing grossly between benign and malignant lesions cause an extension of the indication for resection. This is the attitude that Wilensky and Thalhimer took.

Möller's[302] review of 147 cases of gastric cancer showed that only 13.4 per cent of the 83 patients, who survived the operation, have lived for periods up to sixteen years. Considerable improvement in these statistics ought to be possible if the diagnoses were made early and the patients were submitted to operation while they were still in fairly good condition.

In 1907, Moynihan was able to find 17 cases in the literature of *total gastrectomy;* 3 doubtful cases are included in this list. Hartman[307] reports another case this year operated upon by W. J. Mayo. Both Mayo's patient and Moynihan's patient later developed a condition of the blood simulating pernicious anemia.

THE DUODENUM.

Chronic Duodenal Obstruction.[314–322] According to the Kelloggs,[314] Quain,[317] Crouse,[322] and others, chronic duodenal obstruction is a commoner condition than is realized. Ssokoloff, writing from Russia, believes that the condition is also on the increase and attributes the latter to the undernourished state of the Russian people.

There are two types of duodenal stenosis: (1) That which results from tissue contraction due to ulcer, and (2) that due to periduodenal adhesions of duodenal or other origin. Bode[318] points out that only such adhesions which hinder the mobility of the duodenum call forth pathologic phenomena. Besides adhesions of the duodenum to the under surface of the liver, there may be others to other adjacent structures which cause almost an hour-glass constriction of the duodenum. The Kelloggs[314] point out that the obstruction may involve the first two portions of the duodenum; involvement of the entire duodenum is most frequently caused by compression between the vertebral column behind and the superior mesenteric vessels in front, especially when there is traction downward from the drag of distended and ptosed cecum and colon.

Leveuf[319] has made an analytical study of the reported cases of compression just referred to. The cases seem to be of two types. In one, the stomach is either not dilated at all or only slightly dilated, while in the second, gastric dilatation may be very formidable. When a "giant" duodenum is present, it indicates that the pyloric sphincter has preserved its tonicity. More than half of the cases have their origin in some congenital abnormality. The others are secondary to a dilatation of the stomach which, as a rule, is associated with a general ptotic state. Corresponding to both chronic types there are a variety of intermediate clinical forms. In Wheelon's[316] case, gastric motility was of sufficient strength to cause dilatation of the duodenum.

The physical signs of obstruction in the first portion of the duodenum are those of pyloric obstruction. When the other parts are involved, the Kelloggs[314] indicate that the *x*-ray is inconclusive; they make use of a special form of percussion.

The symptoms are those of epigastric discomfort and toxic manifestations. The Kelloggs attribute "bilious attacks" to this lesion. When gastroptosis is so marked that it angulates the first part of the duodenum, *temporary forms of duodenal obstruction may occur* according to Davison.[320] These occur at intervals varying from a few hours to several days. During such attacks, there is paroxysmal pain in the epigastrium, vomiting, and bilious regurgitation; sometimes the vomitus contains blood. The attacks subside after free emesis. As a rule, an Ewald test-meal shows a high acidity and the absence of lactic acid, Boas-Oppler bacilli, and sarcinæ. There is usually a slight leukocytosis.

Leveur[319] recommends that conservative forms of treatment be practised before operation is considered. Surgical treatment for obstructions in the first two portions of the duodenum consists of the freeing of adhesions, gastropexy, or duodenoduodenostomy. In the third portion of the duodenum the procedure of choice is duodeno-jejunostomy. All the writers recommend, further, that a search be made for any other form of disease in the belly, and that, when present, the latter be corrected at the same sitting. Well-marked cases of this lesion due to the various causes indicated seem to reflect a well-established clinical entity well worth one's attention. In those cases, however, in which neither the clinical picture nor the operative findings are sharply marked, one obtains the impression that the matter degenerates into one of those undefined obscure affairs in which an exploration, with a failure to find any definite lesion, is the result of the laparotomy and in which a successful result of the various operations recommended is a hope or an accident.

The operation of duodenojejunostomy, referred to, is a procedure which seems to have a certain sphere of usefulness in (*a*) vicious circle after gastroenterostomy; (*b*) accompanying gastroenterostomy when the duodenum is obstructed; and (*c*) in the condition described by the Kelloggs.

Carcinoma of the Duodenum.[323-325] Clinically, the most valuable classification of carcinomata of the duodenum depends on the relation of the tumor to the ampulla of Vater; Fenwick and Bland-Sutton so group their cases. I went into the frequency of this condition last year.

The relationship of supra-ampullary carcinoma of the duodenum to a preëxisting ulcer is of great importance. Herman and von Glahn[325] are of the opinion that such carcinomata can occur independently of any preëxisting ulcer; and they quote Judd to the effect that there is little evidence of duodenal carcinoma ever arising from an ulcer. Generally, this relationship has been considered as rare.

Apparently, this opinion is not quite correct according to Meulle[323] since he found that the tendency to malignant change occurred in 50 per cent. This seems to correspond with the proportion in a series of cases from other clinics. Kuttner found that a similar change was

present in 13 of 30 cases of duodenal ulcer; and Kelling found it also in 8 of 11 cases of callous ulcer.

The rarity of cancer of the duodenum developing from ulcer may be accounted for by the fact that there is a greater infrequency of callous ulcer of the duodenum than of the stomach. In view of these facts, further research is necessary to ascertain if carcinoma of the duodenum is really as uncommon, either numerically or proportionally, as it is generally supposed to be.

THE SMALL INTESTINE.[321–334]

Another case of SIMPLE ULCER OF THE SMALL INTESTINE is reported by Basile.[326] This is an uncommon lesion. Loretta, whose paper I reviewed last year, was able to collect only 22 cases from the literature. In their morphologies, these lesions have resemblance to "peptic" ulcer of the stomach or duodenum.

In doing *resections of the small intestine*[327–328] a closed cavity is always left when the seroserosa suture is applied. Robineau[327] gives a description of a method whereby this is avoided. The essential part of the technic is to suture the layers of the bowel wall separately: one layer for the mucosa, and one for the muscular and serous layers. The technic takes time and patience, and clamps cannot be used with it.

Twenty-one cases of *multiple resection of the small intestine*[327–328] are collected from the literature by Hunt. The only successful case was the one of Hunt;[328] there were three resections in this case, each done with a Murphy button. Hunt's recommendation to do multiple resection when too great a length of bowel would have to be removed if only a single resection were done, does not agree with the majority opinion; the latter teaches that the shock with multiple resection would be infinitely greater; the statistics which Hunt quotes bear out this statement.

The studies of Sabin[329] showed that in *end-to-end anastomoses* of the intestines the infolded portion of the wall does not necessarily die and continues to function; nor does it block the lumen. The muscularis mucosa is very sensitive to injuries of any kind, including the application of clamps. The same applies to the other smooth muscle layers. No dilatation of the gut was noticeable. All of the cases showed gaps in the musculature where the stitches were applied and from which they, later, were pulled out, but this, naturally is unavoidable.

The Appendix.[335–356] Everyone is interested in the *results of operations for chronic appendicitis* because everyone has seen numerous individuals who have complained of right-sided abdominal symptoms, or who have suffered more or less from digestive disturbances, in whom the operation of appendicectomy has been unsuccessfully done in the hope of a cure. Numerous experiences of this kind are suggestive that a little more conservatism should be exercised in advising the removal of the appendix.

The statistics of Barclay and McWilliams,[335] which are reproduced from their paper are instructive:

TABLE I.

200 Operations for chronic appendicitis in the Presbyterian Hospital, New York City (1916–1917).
           146 females . . . . 73 per cent.
           54 males   . . . . 27 "   "
1. Cures in 151, or 75.5 per cent.
2. Improvement (satisfactory), but not perfect cures in 22 (11 per cent).
        1. All but 2 had pathologic appendices.
        2. In 15 no ascertainable causes for lack of cures.
        3. In 7—
                 Movable kidneys. 2.
                 Uterine (adnexal) lesions, 5.
3. Failure to cure, 27 (13.5 per cent).
        1. All but 1 had pathologic appendices.
        2. In 10 no ascertainable causes for lack of cures.
        3. In 17—
                 Dilated, movable ceca, 1.
                 Kidney, movable, 1; calculi, 3.
                 Uterine, 6
                 Adhesions, 3.
SUMMARY OF UNCURED CASES (2 AND 3 ABOVE).   Total of 49 (24.5 per cent).
1. Pathologic appendices in all but 3.
2. No ascertainable causes for lack of cures, 25–51 per cent.
3. 24–49 per cent had—
                 Movable, dilated ceca, 5.
                 Kidney, movable, 3; calculi, 2.
                 Uterine and adnexal lesions, 11.
                 Adhesions, 3.
No subsequent hernia in scar in any case.
No subsequent inguinal hernia in any case.
Pain before the operations the only symptom in 51 per cent of the 200 cases, with
    71 per cent of cures.
Pain with stomach symptoms in 49 per cent of the cases, with 80 per cent of cures.
Diarrhea in only 5 instances.
Constipation the rule.

TABLE II.

58 private patients unrelieved of symptoms after appendectomies.
Causes of unrelief:
          2 gastric crises.
        43 splanchnoptosis.
          1 ureteral calculus.
          2 pericolic adhesions.
          5 duodenal ulcer.
          4 gall-bladder disease.
               Infection, 1.
               Calculi, 3.
          1 chronic duodenal obstruction.

Two facts are pointed out by Barclay and McWilliams:[335]   (1) That the hospital patients are being examined more carefully than private patients; and (2) that among the private patients the greatest number of mistakes have occurred among the so-called visceroptotics. The maximum amount of conservatism ought to be exercised in operating upon the latter patients.

The association of chronic appendicitis with gastric or duodenal ulcer, or with gall-bladder affections is so common that it does not seem wise to neglect to remove the appendix when operating upon these latter conditions.

These experiences of Barclay and McWilliams[335] confirm those of Gibson.[5] The latter found that by doing more thorough explorations

the percentage of failures after so-called chronic appendicitis operations has been diminished. These experiences, furthermore, correspond with those of Zweig[336] and of Agote[337] and, as a matter of fact, with that of any one doing any considerable amount of abdominal surgery.

ETIOLOGY OF APPENDICITIS. Wilkie[338] classifies his appendix cases into (1) acute inflammation of the appendix wall; (2) acute obstruction of the lumen; (3) perforating ulcer of the appendix wall; and (4) acute inflammation with secondary acute obstruction. In animal experiments, Wilkie simulated an obstructive lesion. When, under such conditions, the appendix was left empty, a mucocele formed; when it contained a small amount of fecal matter, an empyema resulted which finally ruptured; and when a considerable amount of fecal matter was contained in the appendix, gangrene rapidly ensued. The close resemblance between these experimental changes and those in appendicular disease in the human subject lead Wilkie to assume that obstruction was the primary (I should say, important) factor.

I referred last year to the subject of *intestinal parasites as causes for acute appendicitis*; and this year Marulanda[341] continues in much the same spirit. A communication of Fischer,[340] however, contradicts this. Among the Chinese intestinal parasites are extremely common, but cases of acute appendicitis are rare, even though among the Europeans in China the number of cases are proportionally the same as in the European environment.

Watson-Williams[342] claims that accessory nasal sinus infection is not infrequently associated with appendicitis; no less than 14 of 90 cases of this disability (15.5 per cent) had undergone appendicectomy. This seems to indicate that the accessory nasal sinuses are harboring foci from which infection is derived in abdominal disease.

APPENDICULAR SYMPTOMATOLOGY AND DIAGNOSIS. Caplesco[343] describes a group of cases of appendicitis in which a mild form of *jaundice* is present. The patients suffer from dyspeptic disturbances of various sorts. The jaundice is said to be of a toxic origin. There is sufficient ground here to question whether two coexisting conditions are not being confused.

Baetjer and Friedenwald[346] found the *roentgen ray* of value in the examination of certain instances of acute appendicitis. I should think that there would be a certain amount of danger connected with this unless it were simply limited to distinguishing between a beginning pneumonia and an acute appendicitis. In chronic cases, the fluoroscopic examination, combined with palpation, is especially valuable. Tenderness immediately over a fixed visualized appendix, the kinking of which remains constant, and persistent upward turning of the organ are fairly diagnostic features in Baetjer and Friedenwald's[346] experience. In certain cases, however, they emphasize that the roentgen-ray examination does not give positive information and may even be misleading.

Bennet[345] is more conservative; he urges the consideration of the effect of a large mass of barium in any portion of the alimentary canal and the violence to which the ileocecal region is frequently subjected by massage, palpation, etc. Bennet refutes the claims of some men in regard to the

clinical value of visualization of the appendix by the following table of 50 cases subsequently operated upon. Of 22 visualized appendices, 20 were diseased and 2 were normal. Of 28 invisible appendices, 15 were diseases and 13 were normal. In 15 consecutive postmortem examinations, preparations were made of the bowel in the cecal region and barium was poured into the cut end of the ileum. In 4 diseased specimens the barium overflowed into the appendix; of the remaining 11, which apparently were normal, there was no overflow in 7, and the other 4 filled as readily as the diseased specimens. The visibility of the appendix during a roentgenologic examination cannot be of decisive moment.

McWhorter's[348] reference to a type of *non-perforative appendicitis causing peritonitis* interests me very much. This is a type of inflammation in which the infection passes through the appendix wall without leaving much evidence in the appendix itself, or in which the seat of the lesion is under the peritoneal coat. The importance of this type of appendicitis lies in the fact that when such a lesion is uncovered at operation, it is important to make sure that no other lesion is present competent to produce the peritonitis. I am minded of a young girl upon whom I recently operated in whom, at a secondary operation, tubo-ovarian abscesses were found.

In a general way, it is well known that the appendix is an infected organ. Farr's[349] laboratory work has some relation to McWhorter's[348] observations and deals with the bacteriology and *bacterial count* of the exterior of the appendix and the meso-appendix. The number and variety of infecting organisms may be noted in the accompanying chart. The observations lead Farr to believe that the appendix is a contaminated organ, even when not the slightest sign of inflammation is visible.

Farr's[349] studies also have bearings on the problem of healing in wounds that are sutured without drainage. The table is self-explanatory.

Kraft's[350] studies are complementary to those of Farr.[349] They deal with the bacteriology of the interior of the appendix. It is interesting to note that hemolytic streptococci occurred in his series in nearly equal proportions in normal and diseased appendices. The trouble with such studies is that the true infecting organism is so quickly overgrown that it is difficult or impossible to make a proper judgment.

Brown and Cade's case[351] in which a positive blood culture was obtained during an attack of appendicitis is most uncommon.

The *late results* of cases of *acute appendicitis*, as shown by Bancroft's[352] figures taken from the New York Hospital, are interesting. Secondary abscesses developed in 6.7 per cent of the abscess cases, and in 7.8 per cent of the "fluid" cases (those with peritoneal exudate) of which one-half had not been drained. Hernia occurred in 18.7 per cent of the abscess cases, and in 5.5 per cent of the "fluid" cases. Of the undrained cases, 1.9 per cent developed hernia, and of the drained cases 15 per cent. Prolonged drainage seemed to be an important factor favoring this sequel. Fecal fistula developed in 11.2 per cent, and ileus in 1.5 per cent of the abscess cases, while none of the cases with peritoneal exudate showed this complication.

Dr. Chas. E. Farr, 131 cases.

	Gram-neg. bacillus of colon group.	Same + Gram-positive cocci.	Same + diphtheroid bacillus.	Same + Staphylococcus albus.	Same + Staphylococcus aureus.	Same + non-hemolytic streptococcus.	Bacillus coli communis.	Same + Staphylococcus aureus bac. proteus.	Same + Bac. lactis aërogenes.	Same + Staphylococcus albus.	Bacillus coli communior.	Staphylococcus aureus.	Same + non-hemolytic streptococcus.	Diphtheroid bacillus.	Bacillus pyocyaneus.	Staphylococcus albus.	Same + diphtheroid bacillus.	Gram-neg. bacillus producing no gas and fermenting no sugar (contaminated)	Bacillus alkaligines.	Bacillus proteus.	Contaminated with bacillus subtilis.	Contaminated.	No growth.	Total.
Chronic appendix. Primary union	17	1	1	1	2		4	1			3	1		3	2	1			3		3		7	50
Chronic appendix. Hematoma of wound	1																							1
Prophylactic appendectomy. Primary union	14						4			1		1		2		5	1			1		2	2	33
Prophylactic appendectomy. Hematoma of wound or abscess of wound			1											1										2
Acute appendix. Primary union	13						2		1		1	2		3		1		1	1	1	1		7	34
Acute appendix. Drained wounds	3					1	1						1							1			2	9
Acute appendix. Seventh-day infections	2																							2
Total	50	1	2	1	2	1	11	1	1	1	4	4	1	9	2	7	1	1	4	3	4	2	18	131

I have reviewed and discussed the subject of CARCINOMA OF THE APPENDIX in previous numbers of PROGRESSIVE MEDICINE. There are several new reports this year (Wilkie,[359] Gerlach,[358] Perret[357]). Carcinoma of the appendix is a relatively benign lesion; Aschoff, doubting whether they are real tumors, called the lesions mucous membrane nevi. McKenty calls attention to the fact that no authentic case of metastatic growth following an appendix carcinoma is on record. Gerlach[358] distinguishes between the true carcinomata of the appendix, which are very rare and show all of the characteristics of an ordinary intestinal cancer, and a benign group of tumors which he calls choristomata—more commonly called carcinoids. The latter occur in young persons, never exceed a certain small size, never show metastases or recurrences, and differ in their histologic structure from true carcinoma; they are not early stages of true cancer.

Goldstein[360] has collected 17 cases of *primary sarcoma of the appendix*. The clinical picture has always been that of an acute appendicitis. Masson[361] has had 10 cases in which an actual *neuroma in an obliterated appendix* was found to explain the symptoms.

Lipoma of the Intestinal Tract,[367, 368] Carlucci[367] summarizes the available knowledge in regard to lipomata of the intestinal tract. Lipomata may develop from the submucous coat and grow inward, or from the subserous layer and grow outward. They may occur anywhere along the intestine but seem more common near the ileocecal valve. They are usually single, but may be multiple. They vary in size and in gross morphology, being smooth, nodular, or lobulated. Odelberg[368] has had 5 cases in the jejunum and ileum. The clinical symptoms are usually obscure or entirely wanting until the growth acquires a size sufficient to cause mechanical disturbance with the bowel function. Intussusception is common.

Sarcoma of the Small Intestine.[369, 370] Cases of primary sarcoma of the small intestine are reported this year by Telling[369] and by Perez.[370] In Perez'[370] case the metastases were confined to the nearest lymph glands of the mesentery. Several cases are in the literature in which under similar circumstances the removal of the major focus caused a retrogression of some smaller secondary foci which had not been removed. Sarcoma in the small intestine differs from sarcoma elsewhere in spreading by the rich lymphatic plexus of the mesentery.

Intestinal Stricture and Pernicious Anemia. Meulengracht[371] summarizes 5 cases of pernicious anemia which were apparently associated with a benign stricture at one or more points of the bowel during life. All but 1 of the cases are from the Scandinavian literature. This coincidence of bowel stricture and pernicious anemia seems to be more than casual. The strictures seem from their descriptions to be replicas of old healed tuberculous ulcers; there was no evidence of any recent infection. The diagnosis was made during life in the English case only. The stagnation and decomposition of feces above the stricture with absorption of toxic substances through the bowel wall which had a destructive action on the blood constituents, is the explanation vouchsafed for the development of pernicious anemia.

Intestinal Obstruction.[372-405] Haidenhain first described spastic ileus[382-385] in 1897. In 1902, Langenmak was able to collect 12 positive cases. Last year, Sohn could collect only 30 cases. Fromme distinguished five groups of cases: These differ essentially in their etiology, but the individual phenomena naturally do not differ markedly. Some of the cases may also be due to intestinal paralysis. Pototschnig[382] suggests as etiology the Littre hernia and embolism of a mesenteric or omental vein. The various etiologic factors point to involvement of the autonomic system with its tendency to spasm.

Bowel spasm caused by internal or external irritation (reflex spasm) is distinct from that due to nervous causes (nervous spasm). Chief among the external causes of reflex spasm are dull injuries of the abdomen. Spasm following operation is undoubtedly due to small emboli from thrombosed mesenteric vessels. (I wonder how much this latter cause is operative for the ordinarily-seen, postoperative distention, especially in the severer forms.) Internal irritation, which is much more common than external irritation, is due to the presence of foreign bodies in the intestine or inflammatory processes in the bowel wall, or both. Gall-stone ileus is really an obstruction ileus plus spasm ileus. Spastic ileus associated with the presence of worms is due to the irritation by chemicals contained in the intestines and genital organs of the parasite.

The purely nervous spastic ileus in which a primary competent cause cannot be distinguished must be regarded as a manifestation of hysteria or neurasthenia. Sohn[383] divides this form into pseudo-ileus, spastic ileus and paralytic ileus but it is often most difficult to distinguish them apart. Little is known concerning the etiology of this form of disease; it is worthy of note that these spasms do not relax under anesthesia and can be found even at autopsy; the small bowel and the sigmoid are most frequently involved.

When the spasm is situated in the jejunum, the symptoms must be differentiated from those of acute dilatation of the stomach and arteriomesenteric thrombosis. The condition usually persists for several days before it proves fatal. As a rule, the formation of a jejunal fistula or an artificial anus causes the disappearance of the spasm. Occasionally it persists in spite of the fistula for weeks or months. When the cause lies in the central nervous system, the condition runs a chronic course. In most cases there is tachycardia, occasionally bradycardia. A positive diagnosis is possible only at operation. The anatomic findings are intestinal spasms, which vary in extent and location. As a rule, it is found in the lower ileum. The large intestine is rarely involved. The spasm may appear simultaneously at various points, or, intermittently, at one area. In the spastic areas the intestine is firm and anemic, while in the other portions it is distended and relaxed. The line of demarcation is always distinct. The findings at postmortem examinations are similar.

The prognosis is always good in the mild cases, and bad in the severe ones. Laparotomy is necessary in the latter. During the operative manipulations, relaxation of the contracted areas are to be observed.

Atropine, morphine, chloral hydrate, bromides and heat may be given either alone or with the operative treatment. Surgical therapy consists in the formation of a jejunal fistula, artificial anus, or entero-anastomosis, with, or without, resection. The danger that spasms will again occur remains.

A form of SPASTIC ILEUS is described from French sources which is A MANIFESTATION OF EPIDEMIC ENCEPHALITIS. There were definite evidences of cerebral involvement in Mauclaire's[384] case. The occlusion is evidently of a spastic nature and is apparently due to a form of traumatic injury of certain parts of the intestine provoked by the incessant contractions of the diaphragm and muscles of the abdominal wall. I called attention to this myoclonic condition of the diaphragm last year in speaking of the surgical complications of epidemic influenza. The myoclonic rythmic jerkings and twitchings of the abdominal wall and diaphragm was a dominant phenomenon in Kummel and Fol's[385] case also. In several of the reported cases the condition was misinterpreted, and the patients were subjected to unnecessary operation.

Forty-four per cent of the cases of INTESTINAL OBSTRUCTION operated upon in the Rehn clinic[372, 373] are DUE TO BANDS AND ADHESIONS. Cases in which the condition followed operation are twice as numerous as when no operation preceded. During the last two years there has been a greater frequency of cases of intestinal obstruction and this has been attributed to the war diet and the consequent decrease of mesenteric fat. Flesch-Thebesius,[372, 373] however, ascribes the increased frequency (1) to the method of skin preparation with tincture of iodine which, entering the abdomen, encourages exudative processes in the serosa; (2) to the introduction of ether into the abdominal cavity; (3) to tamponade; and (4) to extravasation of blood. Such adhesions disappear spontaneously in the great majority of cases, but, occasionally, produce pathologic kinking of the intestine.

Flesch-Thebesius[372, 373] does not favor the use of substances such as sterile oil, fluid lard, and ether to prevent adhesions, but recommends the stimulation of peristalsis by the injection of physostigma, enemata, and by the application of heat. In the Rehn clinic, this treatment has reduced the number of cases of postoperative ileus to a low figure (22 cases in 1800 in four years).

In 113 cases of postoperative ileus operated upon in the Rehn[372, 373] clinic in the past fifteen years, the primary operation was for appendicitis in 69. Ileus usually occurs within four weeks of the primary operation, but in some cases it may not develop until as late as ten years later. As a rule, occlusion of the bowel results from the formation of broad adhesions between loops of bowel or between the latter and the parietal peritoneum. In some cases there may be adhesions to the drainage apparatus, and, therefore, drainage ought to be dispensed with as soon as possible. In the Rehn clinic the patients recover in 73 per cent of the cases.

In Flint's[386] series of 282 cases, the mortality was 15.6 per cent for all varieties of ileus including strangulation, external herniæ, and acute obstructions from carcinoma. Leaving these out of account, there

were 70 cases with a death rate of 28.5 per cent. The mortality of all cases not requiring resection was 9.3 per cent. The mortality following resection was 45.4 per cent. In Finney's[357] series of 245 cases, the mortality-rate was 36 per cent. From the study of the different operations performed and the circumstances under which they were done, Finney believes that the results depend more upon the patient's condition at the time of operation, the length of time since the onset of the symptoms of obstruction, and the condition of the bowel, than upon the nature of the operation itself. Other factors being equal, resection seems to compare favorably with the simpler forms of operation. The mortality rate was 5 per cent for those operated upon in the first five hours; 11 per cent for those operated upon in the second twelve hours; 31 per cent for those operated upon in the second twenty-four hours. The mortality in cases of obstruction following strictly pelvic conditions was over 50 per cent.

The mortality of enterostomy in Finney's[387] cases was 60 per cent, but this high rate can be attributed to the fact that operation was done only in the most extreme cases, Wortmann's[388] mortality for enterostomy was 34.4 per cent. In resection of the intestine, which was generally followed by entero-anastomosis and, occasionally, by enterostomy, the mortality in Finney's cases was 33 per cent. When the viability of the gut is doubtful and the patient's condition such as to justify it, this latter technic is Finney's choice.

The gravity of intestinal obstruction is due to three factors: (1) The arrest of the fecal current; (2) the interference with free circulation in the segment obstruction; and (3) constitutional symptoms due to resorption of poisonous intestinal bodies. Finney calls attention to the difficulties of an early diagnosis in postoperative cases when they are masked by symptoms usual to an immediate postoperative period. The important points in these cases are: to recognize those that do not respond to gastric lavage, enemata and the proper administration of cathartics, and in which the symptoms are of a progressive nature; and to reopen the abdomen before irreparable damage is done.

The following facts concerning acute intestinal obstruction may be stated as generally believed:[389]

1. The cause of death in acute obstruction is a form of chemical intoxication.

2. The toxic chemicals are developed in the process of protein disintegration.

3. The effect of these toxic chemicals is to cause a fall in blood pressure, temperature disturbances, vomiting, diarrhea, disturbances of kidney excretion, high non-proteid blood-nitrogen, delayed coagulation time of the blood, profound congestion of the duodenal and jejunal mucosa, collapse and death.

The following points are in dispute:

1. The precise chemical nature of the chief toxic factors.

2. The precise cause, bacterial or other, of the protein disintegration that results in toxin production.

3. The concise mechanism of absorption.

There is forced upon the mind of anyone who examines a considerable series of cases of this condition one conclusion which is of the utmost significance. Van Beuren[375] puts it mathematically; subject to certain exceptions it may be stated as a fact that, if the case is one of intestinal obstruction, the longer the patient lives with it before operation, the sooner he dies afterward.

There are several good reasons for urging early operation which are familiar to all of us. The statement of Van Beuren[375] is one of them. Then the longer a patient is unrelieved of the ileus the greater the fluid loss from the body, the poorer the circulation, the greater the prostration and the worse the general condition. It is probable, too, that the poisonous quality of the gut contents becomes enhanced with time. And it is unquestioned that the damage to the gut itself increases the longer the gut is obstructed. The last is very important, as in Van Beuren's experiments in animals the mortality rate increased in direct ratio with the extent of the bowel damage.

The value of BLOOD CHEMISTRY IN THE EARLY DIAGNOSIS OF ACUTE INTESTINAL OBSTRUCTION[390, 391] was stumbled upon by Tilleston and Comfort in 1914, and was taken up by Cooke, Rodenpaugh and Whipple, in 1916, who investigated the subject from an experimental basis. The latter were of the opinion that the determinations of the non-coagulable nitrogen was of more importance than the blood urea nitrogen. Mc-Quarrie and Whipple found that there is impairment of the excretory renal function, as shown by a decrease in the ratio of urea and sodium chloride excretion and a decrease in the percentage output of phenol-sulphonephthalein. The decrease in the latter is not so pronounced and a marked decrease in the output of the dyestuff occurs immediately before death.

Corroboration of this experimental work is found in the clinical investigations of Louria[390] and of Rabinowitsch[552] in cases of intestinal obstruction. If further clinical evidence is forthcoming, the method ought to prove valuable as a preoperative guide of the degree of intoxication and a postoperative guide of the prognosis. Rabinowitsch[552] attempts to draw conclusions from the high figures found for blood urea nitrogen as opposed to a coexisting fairly normal renal function: the maintenance of such a combination indicates, in his experience, an unfavorable prognosis in spite of the amelioration of the clinical symptoms.

The problem that confronts the surgeon in every case of obstruction is the emptying of the intestinal canal. When free drainage is once established, the patient's urgent symptoms are relieved; the cause of the obstruction is a matter for later concern. *Enterostomy*[392, 393] accomplishes this primary indication. In all instances surgeons select usually for this purpose the first or most accessible coil—Nelaton's advice. Victor Bonney, in 1910, advised that instead of following Nelaton's injunction, the jejunum be opened. Hugh McKenna, in 1913, supported this advice with animal experiments and clinical cases. He used the Nelaton-Bonney technic, a type of operation which frequently requires a secondary operation for closure and which permits a wastage of stomach

nourishment. Instead of this, McKinnon,[392] in 1917, and again this year, recommends strongly the doing of a simple modern jejunostomy. McKinnon[392] is very enthusiastic about the operation; in his experience, a properly performed operation, "will drain the intestinal canal, reduce intra-abdominal tension, improve respiration—all this with surprising suddenness."

Summers[393] feels sure, from personal experience, that, unless the vomitus is frankly feculent, the tube ought to be introduced into the highest segment of distended bowel and not into the highest part of the jejunum.

From the various enthusiastic reports, this type of jejunostomy seems to be a distinct advance. There is a report in the German literature by Vollhardt[553] which confirms this opinion.

A method of *intestinal intubation through an appendix stump* is described by Collins.[554] This is adapted only to cases of appendicitis with peritoneal involvement.

Ileal Regurgitation. Chronic Intestinal Stasis.[406-420] In unselected gastro-intestinal cases, Bryant[406] expects to find from 20 to 30 per cent of the cases of *ileal regurgitation*. The patient usually suffers from an increased intensity of any nervous complaint to which he may be liable. Roentgenographically, according to Baetjer and Friedenwald,[407] the condition is indicated by the fact that at the end of twenty-four hours, after the barium contrast meal, the ileum is empty and at the end of from thirty-six to forty-eight hours the terminal ileum fills again. The entry of an opaque enema into the small intestine is not an absolute proof of this condition owing to the factor of pressure in introducing the enema. Ileal stasis may be due to spasm, ileocecal valve incompetency, bands, displacements prolapse and tumors; dilatation of the terminal part of the ileum usually points to obstruction.

In some instances these abnormalities are associated with chronic appendicitis, and both of the conditions may be due to a low grade of inflammation. Dilatation of the cecum may be present, even when the bowels move regularly every day.

Donati and Alozna[555] devote much study to a *relative stenosis in the ileum or colon*. They trace the cause to a pericolic membrane, or to adhesions of inflammatory origin. The clinical picture includes ileocecal pain and chronic constipation.

Lane's[413] conclusions from twenty years of study of the subject of *chronic intestinal stasis* is not materially different than those we have hitherto heard from him. Because of the seriousness and questionable results, colectomy, which Lane recommends, has not been generally acceptable to most authoritative men for the indications made by Lane[413] and by others. Sheen[557] divides the patients into three classes: (1) Those who recover and are greatly benefited (it is very difficult to obtain truly accurate conceptions of the relative numbers in this group); (2) those who die (complete colectomy is an operation of great magnitude); (3) those who neither die or recover, but live in almost hopeless discomfort.

Ileocolostomy, the suggested alternative for colectomy, is surgically unsatisfactory because of the dead excluded loop which is left. Various

other operations may be, and have been, performed, and toxemia previously present may disappear. The good results of such operations Sheen[557] believes to be due to the freeing of the ileal effluvient. The treatment of these intestinal disorders is most unsatisfactory. Under the present circumstances, every patient ought to be treated in accordance with the special symptoms presented. Surgery is not the only remedy and is, perhaps, the last remedy to be considered. In both medical and operative treatment, the psychic factor is most important and must not be overlooked. Decent methods and habits of living commenced in early life are most important prophylactic measures.

THE COLON.[415, 421—448]

Congenital Idiopathic Dilatation of the Colon is the most comprehensively descriptive title yet suggested for *megacolon*. Hawkins suggestion of some neuromuscular defect as a cause for this congenital condition is worthy of further investigation. Ladd's[415] summary of this condition is very good. Pathologically, there is present an enormous dilatation, usually involving the sigmoid and descending colon, beginning and ending abruptly and with a marked thickening of the bowel wall. The basis for the latter is a hypertrophy of the mucosa and muscular layers, with some increase in connective tissue.

Clinically, the story is one of constipation, with accentuation upon the long periods of time that the child can go without a bowel evacuation. Attacks of distention are frequent, and are dangerous because a fatality may occur during one of them. The attacks are accentuations of the ordinary state of affairs in these unfortunates and usually accompany an increase in the toxemia.

The medical treatment of this condition was referred to last year. It may be said to be that of constipation and is not very satisfactory. The surgical treatment has been varied. *Plication of the enlarged colon* has been performed with no benefit. The results of *fixation of the colon* do not warrant its further consideration. *Short-circuiting operations* have also been tried unsuccessfully. The two operations which are worthy of consideration are *colostomy* and *resection of the affected loop*. The latter operation is the one of choice; the other the one of necessity. Lateral anastomoses should be selected in preference to end-to-end unions.

Postoperative Intestinal Disease. Goldschmidt and Mulleder[421] found that an *enteritis* was present in 29.3 per cent of the cases after extensive operations on the stomach, the pathology resembling that of dysentery. The material consisted of 203 operative cases. The intestinal lesions are probably secondary to the changed chemistry of the stomach. The therapeutic use of hydrochloric acid is strongly recommended and corresponds to the postoperative demands of acid food.

Dysentery.[422—426] Large epidemics of dysentery, especially of the amœbic variety, are rare in the temperate zones of the world, although small outbreaks have been known to occur. The latter break out under the unusual conditions of army life, such as the one in East Prussia in

1901. Dependable information on this subject has, until the last few years, not been forthcoming. The World War created ideal conditions for the dissemination of these epidemic diseases in the intermingling of races and infectious agents in, perhaps, unsuspected ways. These two conditions will undoubtedly make for a very great increase, in the immediately coming years, in the sporadic cases of dysentery and will probably increase the number of cases that develop in the temperate zones and that are not imported from those circumscribed geographic areas where dysentery is common. The figures of Kofoid[422] are impressive: Examinations of the men in the American military establishment showed that 4 per cent of the men in home service harbored endamœba dysenteriæ as against 20 per cent of those in overseas service; this means that we have imported several hundred thousand men into the country with potentialities for spreading this disease among the civilian population.

In stubborn cases of colitis or dysentery, surgery is indicated. In severe cases, however, surgery is not very promising. In extensive necrosis and gangrene of the intestine due to dysenteric infections, surgery is hopeless. Surgery resolves itself into doing an appendicostomy or cecostomy. Appendicostomy is not always possible, but is preferred by Strauss and others; its only possibilities reside in the ability to irrigate the colon. Klose[424] does not consider appendicostomy satisfactory, as it is not possible to empty the intestine satisfactorily through the appendix lumen. Naturally, these two different viewpoints are sponsored by many equally capable men. Most men, however, take the viewpoint that it is a most important consideration to keep the fecal current away from the ulcerated surface. A moment's consideration will convince one that it is not possible to do this through an appendicostomy. For these reasons, it seems to me that a cecostomy is much the preferable operation. I do not think that the objection of Klose,[424] that the total exclusion of the large intestine leads to collapse of its walls, is of much consequence, as the intestine will readily open up again as soon as function is restored; and I do not think it likely that the ulcerated walls will adhere to each other and so close off the lumen entirely; certainly, I have never seen this on the postmortem table. The after-treatment of intestinal irrigation must be kept up for months and is very tedious; correct technic is necessary. If recurrence is to be avoided, the fistula must not be allowed to close, either spontaneously or by operation, until there is an absence of mucus, blood and pus in the stools, until the patient is enabled to digest a full meal without any symptoms or discomfort, until rectoscopic examination shows a normal mucous membrane, until roentgen examination shows a normal motility and until the patient has been free from recurrence for at least three months after the intestinal irrigations and other treatments have been stopped. Such a successful result may be obtained after a few months in some cases, but in others only until after a period of years. I referred last year to the kind of fluid which is best adapted for irrigating purposes; the proper solution is a matter of individual experimentation; usually, the blander the solution is, the better it works.

Intestinal paralysis often occurs during the course of a bad colitis or dysentery. For this indication, Klose[424] did an enterostomy in 4 cases, with good results in only 1.

The *inflammatory circumscribed tumors of the large intestine* which often appear *after dysentery*, and more rarely *after typhoid fever*, should be resected. The sequelæ which so often follow dysentery, such as hemorrhoids, prolapse of the rectum, and volvulus, should be treated along general surgical principles. I reviewed the other surgical sequelæ and complications of dysentery rather fully last year. Bonnet and Michon[425] again call attention to the fact that dysentery can mimic an appendicitis, both symptomatically and pathologically.

Alivasatos[426] describes a form of *non-ulcerative rectocolitis* the prominent symptoms of which are diarrhea and hemorrhage. This form is often tenacious; but under conservative forms of treatment kept up possibly for many months, a cure is usually effected.

Gastro-intestinal Diverticulitis.[427–429]   Gastro-intestinal diverticulitis is an important abdominal condition which does not have the recognition from the surgeon which it deserves. The possibility of diverticula causing trouble depends on three factors: (A) Pressure from within the intestine tends to cause their progressive enlargement; (B) they tend to harbor fecal or other harmful content; (C) they are prone to undergo secondary pathologic changes. The chief secondary pathologic changes are (1) acute inflammation of the sac—diverticulitis; (2) chronic proliferative inflammation with thickening of the intestinal wall and subsequent stenosis of the bowel—peridiverticulitis; (3) chronic mesenteritis of the sigmoid or transverse loop; (4) local forms of chronic peritonitis; (5) the formation of adhesions between the sigmoid loop and other viscera, especially the small intestine and bladder; (6) infection of the general peritoneal cavity from thinning of the sac wall without perforation; (7) perforation of the diverticula giving rise to acute general peritonitis, local abscess, submucous fistula of the intestinal wall. This is the lesion which Hagler[414] is probably describing in his case of dissecting interstitial abscess of the cecal wall, fistulous communication with other viscera or perforation into a hernial sac.

The symptoms are not necessarily due to the diverticula themselves and appear only when these secondary changes take place. Multiple diverticulitis presents a fairly definite clinical picture. In a large percentage of the cases there are attacks of pain of variable severity; in about 25 per cent a history of chronic constipation is obtained; and in about 30 per cent of the cases with symptoms, a palpable tumor is present.

The diverticula may be demonstrated roentgenographically. A preliminary examination is necessary to rule out confusing shadows. The standard test-meal is used. The diverticula are first visualized twenty-four hours later. Some of them are seen by displacing the gut during palpation under the screen. Plates made from thirty-six to forty-eight hours after ingestion of the meal show the diverticula to the best advantage. Roentgenographically, George and Leonard[428] distinguish the following groups:

1. Cases of simple diverticulitis. These are round, discrete sacculations of variable size and number.

2. Cases showing secondary changes of an inflammatory nature. The signs include a beginning narrowing of the lumen of the gut; fixation of the parts from adhesions; and demonstrable rigidity of the bowel wall. Commonly, there is local tenderness.

3. Cases showing advanced secondary changes, such as well-marked pericolitis, tumor with obstruction, etc. Other complications are also demonstrable, such as adhesions to adjacent viscera, chronic perforations, with abscess cavities, or fistula formation. In the cases in the last two groups, it is important to differentiate diverticulitis from carcinoma; naturally, the difficulties are great because of the frequent association of the two conditions.

McGrath[429] speaks of two general classes of diverticula: (1) The congenital and (2) the acquired. It is difficult to explain satisfactorily the pathogenesis of this condition if one leaves out of consideration entirely congenital structural defects. The supposed etiologic factors, other than this, probably play no more than a contributory role.

Of the so-called acquired diverticula, two types have been recognized: (1) The incomplete which involves all of the intestinal layers except the muscularis. This, the most common form, is also spoken of as a "hernia mucosæ." (2) The other variety involves all of the coats of the bowel.

The point which Mellon, Sobel, Davidson and Fowler[429] stress is the apparent predilection of diverticulitis for carcinomatous implantations. From the clinical point of view, this is perhaps one of the soundest arguments for the early apprehension and correction of diverticular formations. These observers outline a number of significant combinations of causes which are present fairly constantly, so that a high percentage of carcinoma might well eventuate under such conditions.

Fistulous communications between the bladder[430–431] *and* various portions of *the intestinal tract* occur with relative infrequency and give rise to definite and distressing symptoms. McKay[558] collected 342 cases from the literature. The chief etiologic causes, besides diverticulitis, are cancer and tuberculosis; in rare cases abscess about the rectum, disease of the appendix, syphilis or actinomycosis are responsible. In the collected cases the opening in the intestinal canal was found most frequently in the rectum, next most frequently in the sigmoid; in the remainder, it was in the small intestine, cecum, or appendix.

The principal symptoms of a fistula between the bowel and bladder are pneumaturia and the passage of fecal material by the urethra. The histories of the Mayo Clinic[431] cases are said to be very similar; that is, an attack of abdominal pain radiating into the pelvis, followed by passage of gas and intestinal matter. Cloudy urine infected with colon bacilli is present almost from the onset. Vesico-enteric fistulæ may be demonstrated in the cystogram. One can frequently see the opening of the fistula in the cystoscopic examination. Stone formation is a frequent complication.

The treatment is purely surgical. After free drainage has been

established, a proper radical dissection, with the removal, insofar as it is advisable, of all diseased tissue is done. In the sigmoid, the fistulous opening is closed over a large rectal tube. The technical difficulties of the operation are the establishment of free drainage and the prevention of pus pockets in an operative field which is always infected. The latter may be cleared up postoperatively by the use of lactic acid bacilli and by irrigations with aluminum acetate solution.[431]

Intestinal fistulæ after operation result from the accidental wounding of the intestines and from suppuration about stitches, ligatures and suture lines. As a rule, such fistulæ close spontaneously after a few weeks, but in some instances they persist and necessitate operative closure. Pauchet[432] advises the following procedures.

Large suppurating fecal fistulæ must be treated by the formation of a temporary artificial anus, and, if the latter does not suffice, by direct operation upon the fistula itself. Fistulæ without pus may be attacked directly. The latter are of three types:

1. Simple fistulæ. Before an incision is made, the course of the fistula is traced by an injection of methylene blue. The intestinal loops are then exposed and the perforation is closed.

2. Fistulæ difficult to expose because they are hidden by adherent intestinal loops. A fistula of this type is traced by inserting a probe. (The methylene blue, it seems to me, would be equally efficacious.) The treatment consists in suturing together two incisions in the loops of bowel in contact with the fistula. By this procedure, the fistula is buried between the two opened loops.

3. Fistulæ of large size. An artificial anus is formed to the left of the umbilicus, and the intestine is completely sectioned. Pauchet has found that placing the lower portion of the colon at rest frequently results in cure. Every eight days the patient is given a copious enema to discover whether any of the water escapes through the fistula. When it ceases, it is assumed that the fistula is closed. I am inclined to believe that an artificial anus would not be entirely successful in many of these fistulæ and that further measures would be necessary.

Multiple Intestinal Polyposis.[433] Multiple polyposis of the intestinal tract is an obscure disease. About one-third of the cases occur between the twentieth and thirtieth years of life and more frequently in males than in females. Symptoms last for many years. The principle complaints are a sense of weight in the rectum, tenesmus, bleeding, diarrhea, vague abdominal pains, colics of obscure origin, partial obstruction and essential hemorrhage. Essential hemorrhage is a nearly pathognomonic sign. Anemia of various degrees are common. The rectum, the sigmoid and the splenic flexure are most commonly involved. The condition is recognizable through the sigmoidoscope in about one-third of the cases.

The surgical methods of treatment include the Brown operation, ileocolostomy, colectomy, ileosigmoidostomy, the Mikulicz operation, the two stage Kraske operation, appendicostomy and the Desquin-Mixter operation. At the Mayo Clinic, [433] the mortality of surgery is 47 per cent. The mortality of medical treatment is about 25 per cent.

The findings at autopsy and operation indicate that multiple polyposis of the intestinal tract is a diffuse disease of the large intestine. Examination of tissue shows that ulcerations are frequently associated with polyposis. This confirms Rokitansky's theory that intestinal polypi arise from dysenteric ulcers of the bowel. The mechanism of their formation is the following: In a large proportion of the cases, there is a progressive general colitis which forms a number of undermining coalescing ulcers; as these heal, the intervening portions of preserved mucous membrane are smoothed off and remain as polypoid projections.

Cancer of the Large Intestine.[6] [434-448] I quote rather liberally from Mayo's[6] remarks. Cancer of the colon has a high mortality and its end-results are not very satisfactory. The death rate does not depend so much on technic as on the character of the case which the surgeon accepts for operation. Mayo finds it difficult to justify this mortality rate but the fact remains that operations performed, even in advanced stages of this malady, have resulted in permanent cures when the condition left alone makes death welcome. The well-known facts that in the normally grossly infected areas of the intestine, carcinoma does not involve the glands early but late, that often when the glands are apparently involved they show only infection, and that the fixation and involvement of the surrounding tissues may still leave the disease local, are the grounds upon which the Mayos do some of their radical operations.

The temptation to perform a permanent colostomy and turn over the bad cases for radium treatment, as in cancer of the cervix, may eventually prove wise, but as yet W. J. Mayo has seen no cures from radium treatment in cases of this description, although great palliation is sometimes secured. Preliminary colostomy for the purpose of cleansing the part to be operated upon, of keeping the wound clean after operation, and especially for the use of radium in the growth before operation, effects a reduction of the mortality and improves end-results. The advantage gained in this manner has, however, in the Mayo's experience, at once been lost by the extension of the operability (*i. e.*, the greater the operability, the higher the mortality).

As regards the actual operative technic, no change is apparent in the literature in the various procedures employed. I went over this aspect last year. In acute obstructions the value of a temporary cecostomy or colostomy is paramount. Radical resections are done at secondary sittings in accordance with findings at the primary operation, and with the amount of displayed recuperating or resisting power of the individual; and are guided by the intervening spread of the disease. Operations are done in one stage when all things concerned are most favorably inclined toward success; otherwise the operation is divided into two or three stages depending on the capabilities, beliefs, skill and experience of the individual surgeon. Operations in many stages seem to have, generally speaking, a lower mortality.

In resecting the colon for carcinoma, a cardinal principle is to ablate that portion lying between the terminal part of the small intestine and a point distal to the carcinoma. In tumors of the ascending colon and hepatic flexure this means the removal of that part of the large intestine

well into the transverse colon. In carcinoma of the transverse colon, this principle still holds good, although there will be cases in which it may seem to the operator that a resection of the transverse portion alone, with direct end-to-end union, is feasible. To carry this principle out to its logical termination would be to endorse the recommendation of Lane[434] to do total colectomy in any and every case of carcinoma of the large intestine. This technic, perhaps, would be ideal from the functional standpoint and from that of the permanent relief from the carcinomatous growth. The difficulties here lie with those malignant tumors growing in the splenic flexure, the descending colon and the rectosigmoid. With such tumors, the removal of the entire large intestine (colon) is an operation of great magnitude and of high mortality. So that discretion becomes the better part of valor and, whenever possible, an attempt ought to be made to obviate the additional risk by doing operations of smaller degree; this, indeed, is the common practise. Luckily, the mobilization of the descending colon and the mobility of the transverse colon are great aids in operations upon the splenic flexure and descending colon, and enable, in a fair proportion of the cases, an end-to-end union after adequate resection. For similar reasons, end-to-end union after resection is the operation of choice in carcinoma of the sigmoid.

Under any condition, the resection should be free and wide. Stretton[440] recommends that at least four inches of healthy intestine on each side of the growth, together with the appropriate mesentery and lymph glands, be removed. End-to-end union is the most favorable method; simple suture is preferable to any mechanical appliance.

Miles[436] points out that the question of the proper method of operation for *carcinoma of the recto-sigmoid* necessitates a knowledge of the manner in which the tumor spreads and the paths it takes in so doing. The early stages of an adenocarcinomatous tumor of the recto-sigmoid are confined to the mucous and submucous coats. The tumor is readily movable on the underlying parts and as it grows it spreads in three directions: (1) By direct extension of tissue; (2) through the venous radicals; and (3) through the lymphatics.

1. The local spread by continuity of tissue is more important clinically than its dissemination through the lymphatic or venous system. For a comparatively long time the disease is, therefore, strictly local. Extension takes place in all directions but more in the transverse than in the longitudinal axis of the bowel. Miles infers that by the time the tumor has gone three-quarters of the way around the bowel, it is approximately one year old. As the tumors so extends, penetration of the growth into the muscular coat is constantly going on; finally it crosses the lymph spaces around the rectum and invades the perirectal fatty tissue and the fascia propria of the rectum. Penetrating fixation to the sacrum, the bladder, the uterus or the vagina is not possible until the fascia propria has been involved, and, according to Miles' inference, for at least one year after the earliest symptoms indicating the presence of the growth. It is important to remember, therefore, that, clinically, such fixation is a very slow process and that its existence is probable and can be

assumed when the tumor has grown around the greater part of the bowel circumference.

2. In spite of this comparative slowness of growth, microscopic specimens afford evidence of the fact that even at a very early stage of the disease there is direct invasion of the venous radicals which afford ample opportunity for emboli to be carried to distant organs, such as the liver. Fortunately, this method of propagation is very rare, and definite liver metastases are generally a late manifestation.

3. The most important route for the dissemination of tumor cells is through the lymphatics. The rectum possesses an intramural set and an extramural set of lymphatic vessels. The spread by the intramural system is of very limited extent. The extramural set of lymphatics is more important. Corresponding to three lymphatic areas there are three zones of spread: (*a*) The zone of downward spread corresponding to the perianal skin, the external sphincter and the ischiorectal fat. (*b*) The zone of lateral spread taking in the levator ani muscles, the retrorectal glands, the internal iliac glands, the base of the bladder, the seminal vesicles, and, in the female, the posterior vaginal wall, the cervix and base of the broad ligaments with Poirier's gland. (*c*) The zone of upward spread including the pelvic peritoneum, the pelvic mesocolon in its entirety, the paracolic lymph glands and the group of nodes at the bifurcation of the left common iliac artery. Early metastases in any of these regions is possible and cannot be detected by the finger. The most vulnerable of these zones include the ischiorectal fat, the levator ani muscles, the retrorectal glands, and the pelvic mesocolon. Therefore, these tissues must be freely removed in an operation for cancer of the rectum.

Surgery, to be successful, must be based on these pathologic considerations. The operations devised to fill these requirements are: (1) perineal excision; (2) perineal resection; (3) vaginal resection; (4) the abdomino-anal operation; (5) the abdomino-perineal operation. Conservative forms of operation in which attempts are made to excise the local tumor-bearing area are to be condemned as a general practise even though from time to time an apparent success is reported in the literature. The first four of the operations named fail because they do not make provision for accurate determinations of the extent of the local growth and the number and location of metastases and their extent.

The radical abdomino-perineal type of operation was planned originally to cover all of these essential points. The technic includes the removal of all of the tissues forming the zones of upward, lateral, and downward growth. A preliminary colostomy is followed by the removal of the entire large intestine distal to the line of section, the rectum encased in its fascia propria, the whole of the pelvic mesocolon, the peritoneum lining the floor of the pelvis with a strip on each side of the parietal attachment of the pelvic mesocolon, the whole of the levator ani muscles, the external sphincter muscle, as much as possible of the ischiorectal fat and a wide area of perianal skin. In the present state of our knowledge this technic seems the best. The operation can be done in one sitting.

Both Lynch[449] and Stiles[452] refer to the value of a preliminary *colostomy*[449-454] or *cecostomy* especially in very bad cases. In a certain percentage of these cases so much improvement occurs in the patient's condition as to make feasible a radical operation at a secondary sitting. Miles also concurs in this belief. Several new methods of making a colostomy were described this year. These, as far as I can see, have no special reason for preference over the many recommended in previous years. The two Burrows'[451] method consists essentially of a subcutaneous channel over the anterior rectus sheath through which the sigmoid is brought out to a second incision some distance from the first. This allows a fair length of bowel which can be compressed externally by a pad. The method of Miles is the usually made spur colostomy which is formed by including in a stout silk ligature the entire width of the mesentery.

In order to make an artificial anus continent, methods similar to those employed in cinematization operations have been devised by Sauerbruch, Ombredanne, Francois, and Unger and Schwalbe. Essentially, these consist of two parallel tubes of skin sunk in the tissues at either side of the new cloaca which are utilized to hold either simple or complicated apparatuses to shut off the intestinal canal; in some of the operations the provision is made for a length of bowel to lie in a subcutaneous channel, somewhat like that indicated in the Burrows'[451] operation, which facilitates the object of the retentive apparatus. A typical example of this type of operation is described by Francois.[559]

Francois cuts rectangular strips of skin on each side of the site of the future cloaca. The free edge of the lower strip is toward the pubis, while the base is toward the new anus and about one centimeter distant from it. In the upper strip, the pedicle is also toward the anus. The axis of each strip is parallel to the anal axis. In the dissection of the strips, fatty tissue is left adherent. The proximal parallel edges of the two strips are sutured together, and, also, the distal parallel edges. Each strip thus forms a free tube, only attached at one end, the epidermis being internal and the fatty tissue external. A button-hole having been made in the skin at the base of each tube, a subcutaneous channel is bluntly bored through on each side parallel to the axis of the future anus. The free end of each tube is seized in a forceps and the tube is drawn through its corresponding channel. Ten or fifteen days later the artificial anus is made by the ordinary technic so that it lies between the two skin channels. A special apparatus is applied about three weeks later. This consists essentially of two thin steel rods covered with rubber and passed into the subcutaneous channels. By an external mechanism connecting them, the two rods can be gently squeezed together so that they close the mucous lips of the anus.

Unger and Schwalbe's[453] method is practically the same as that of Francois. Efficient results are reported.

Prolapse of the Rectum.[454-458] Plenz[454] is opposed to the generally accepted opinion that prolapse of the rectum in children be given ample opportunity for spontaneous healing. He proposes a fascial sling around the anal canal. I should be inclined to wait and hear the final results

before recommending this operation. Ekehorn's method consists in holding up the redundant tissues by means of the scar formed around a stout suture introduced into and through the rectum and out again through the tissues of the buttock. Moller,[456] who applied this method, reported excellent results. I should be afraid that the suture would introduce infection into the ischiorectal space.

The principle of the operation of Mummery[457, 458] for prolapse in adults is to restore the bowel into its normal position in the hollow of the sacrum and to hold it there by firm adhesions. In order to obtain these dense adhesions he makes use of healing by granulation and with this object in view the space posterior and lateral to the prolapsed portion of the rectum is packed with gauze through an incision made between the anus and coccyx. The granulations are only allowed to fill up slowly so as to obtain the strongest adhesions between the rectum and pelvic parietes.

The operation proposed by Richter[455] for prolapse of the rectum is limited to women. Essentially, it consists of passing the divided broad ligaments back of the rectum through an opening in the mesorectum and of fastening them together; of obliterating the pelvic space behind the uterus; and of fixation of the fundus of the uterus in the abdominal wall. Richter's operation has many similarities to the one proposed by Moschcowitz many years ago, the essentials of which are an obliteration of the cul-de-sac. Moschcowitz' operation is, however, not limited to women and can be performed at any period of life. Richter's[455] operation seems to be a modification of the latter toward the side of greater complexity without sufficient additional gain.

Myoma of the Rectum. In an extensive review of the literature, Hunt[459] has been able to find 24 cases of myoma of the rectum since 1872. The infrequency of intestinal obstruction considering the size and location of these tumors is striking.

Sarcoma of the Rectum. Lapeyre[460] collected 32 cases of primary sarcoma of the rectum, only 3 of which were cured by removal of the rectum.

THE LIVER.[461-501]

Effect of Removal of the Liver.[461] The liver, because of its relatively large size, its double blood supply, its secretions and metabolic activities, and, above all, because of its importance to life, continues to be a source of great interest to the laboratory worker and the clinician. For the study of some problems it is desirable to know the course of events consecutive to the removal of the liver. The technic of the latter experimental operation is indicated by Mann.[461]

The operation is performed in three stages. In the first, an anastomosis is made between the portal vein and the vena cava in the manner of an Eck fistula, except that the vena cava is ligated instead of the portal vein. The ligature is applied just proximal to the entrance of the right lumbo-adrenal vein. Three or four weeks later, the portal vein is ligated at the point usual to its ligation in an Eck fistula, after which all the supply of blood from the posterior extremities and the

portal system passes to the heart through the peripheral collateral circulation. At the third operation the liver is removed completely by ligating the hepatic artery, the vena cava just below the diaphragm, and whatever small collateral veins have developed along the gastro-hepatic omentum.

Most of Mann's[461] animals remained in good condition throughout the entire period of observation. After the animal recovers from the anesthetic administered for the third operation, there is an interval—which varied from two to eight hours—during which the animal appears normal. Then it becomes moribund and dies quickly within one or two hours more.

The data so far obtained do not justify many positive statements of the events following removal of the liver. Mann was able to distinguish some change in metabolism whereby some toxic product was elaborated; and that the events showed general similarities to those following removal of the adrenals or parathyroids.

Abscess of the Liver. The proportion of single to multiple abscesses of the liver is put by Reinhold[464] as 3 : 2. The treatment of tropical abscesses has become more medical than surgical since the general use of emetine became established. Reinhold recommends operation when the pus is very foul. If fever and constitutional symptoms persist, and when subsequent repeated aspiration fails to locate further pockets of pus, exploration is necessary through an abdominal incision. The left lobe should be carefully examined when no pus is found in the right. In cases of the latter type, the prognosis is not so good.

Chemically Produced Cholecystitis. Mann[465] has found that the intravenous injection of a solution of chlorinated soda in dogs produces a definite reaction in the gall-bladder in a high percentage of experiments. The reaction consists of a breaking down of the capillaries and infiltration of the wall of the gall-bladder with blood. To produce this reaction, relatively large amounts of solution must be injected (more than 5 cc per Kg.). The reaction takes place very shortly after injection, is completed within the first twelve to twenty-four hours, and is said to be due to the chlorine ingredient. In some instances a definite chronic condition followed the acute reaction.

I referred to these experiments in discussing Rosenow's communication in regard to the elective localization of bacteria. The experiments indicate further that in the last analysis the actual product producing disease of bacterial origin is of a chemical nature.

THE BILIARY SYSTEM.[465 - 491]

Excluding the acute emergencies, the *symptoms resulting from a diseased gall-bladder* for which the patient seeks relief are not all due to the immediate presence of organisms in its lumen or wall. Many of the symptoms are the result of damage to the tract which remains after the infecting organism has been effectively dealt with. That the infecting organism is killed one cannot say; rather, that it becomes encysted in a much depreciated condition and from the latter dormancy it may or

may not be possible for it to resume its natural virulence as demonstrated in a culture tube.[466]

Excluding the acute emergencies, the difficulties in *diagnosis*, which are present, are due to the fact that for a long time gall-bladder lesions meant gall-stones and gall-stone colic. Until one considers the latter only as incidents rather than as essential components of the clinical picture these difficulties will remain. To wait for jaundice and for colic in order to ensure the diagnosis, is, as Graham says, like waiting for metastases before diagnosing malignancy. The diversity of symptoms relieved by surgical intervention in disease of the biliary tract is proved by everyday experience.[466]

The recent tendency has been—and it still continues to be—to rely very much on *roentgen-ray diagnosis*.[468] One has only seriously to attempt this for a few months to realize how difficult and formidable the task becomes. The present pessimism arises from the mistaken notion that the lime content of the majority of stones is so small that their visualization is absolutely impossible. It is not generally appreciated, as Roberts[468] points out, that few gall-stones are devoid of a lime containing layer. I agree with him that there are at present insuperable obstacles to the visualization of every stone, but, as the technic is developed and simplified, the roentgen-ray diagnosis of biliary lesions will be put on a practical and fairly reliable basis. The enlarged gall-bladder can easily be visualized; but, at present, it seems that there will be a small residue of cases of chronic cholecystitis without stones or dilatation which cannot be roentgenographically demonstrated. Dudley Roberts[468] explains that one cannot properly estimate the importance of negative findings on the basis of percentage of failures in a demonstrated series because the latter failures occur in the stout subjects. The importance to be attached to negative findings depends on the character of the roentgenograms secured; in some, the definition of any opinion is not warranted; but a satisfactory series containing an adequate number of pictures with a wealth of detail may warrant a negative diagnosis.

It seems reasonable to assume from the work of Evarts Graham[467] and of Peterman, Priest and Graham, that an *involvement of the liver* is so frequently *an accompaniment of cholecystitis* that the association must be considered practically to be a constant one. The realization of this fact is important for several reasons: (1) Because it can help to explain the exact mechanism and pathogenesis of infections of the biliary tract; (2) because it may prevent many of the serious liver complications which seem to result from neglected biliary tract conditions; and (3) because it may lead to an increase of our knowledge of the whole subject of cirrhosis of the liver and various functional disturbances about which little is known at present.

Present conceptions of the mechanism of biliary tract infections are based on three assumptions: (1) Descending infection from the liver by bacteria carried down the lumen of the common duct; (2) ascending infection from the duodenum; and (3) hematogenous infections. Only the last takes into account the actual infection of the tissues of the

gall-bladder wall; the other two only deal with the entry of bacteria into the lumen of the biliary tract. The additional factors of obstruction to the biliary outflow and some degree of obstruction of the circulation seem to be necessary for the production of cholecystitis according to the first two assumptions; the experiments of Ogata, Rouss and Larrimore and of Chiarolanza seem to support this view.

Peterman, Priest and Graham, and Judd[470] call attention to the experimental work of Sudler. The latter showed that there is a direct and intimate connection between the liver and gall-bladder through the lymphatics which come from the under surface of the liver and pass through the attachment of the gall-bladder to the liver. It is easily conceivable that under these conditions a vicious circle can be established with the liver on the one side and an infected gall-bladder on the other, each being constantly reinfected from the other.

In general, a similar attitude is beginning to be taken with regard to *chronic conditions*. MacCarty and Jackson[469] believe that some of the obscure symptoms can be explained on this basis, as well as some of the recurrences after cholecystectomy or cholecystostomy.

All of these facts make one think that Schnabel[466] must be right in saying that it is largely artifice which leads to a distinction between cholecystitis and cholangitis. Usually, the entire biliary tract is involved in an infectious process, and it is difficult to conceive how the ducts may be affected and the gall-bladder remain free, or *vice versa*. The very close relationship between the integral parts of the biliary system makes it extremely doubtful whether clinically a differential diagnosis can be made between a duodenitis, choledochitis, cholecystitis and hepatitis; and, furthermore, this close relationship would seem to demonstrate the futility of taking out a gall-bladder in some cases if the ducts too are involved in the infectious process.

As regards *pericholecystitic adhesions*, Graham[467] believes that, with the exception of the obvious cases in which they may result from contiguous inflammatory processes, they are an indication of a preëxisting inflammatory process, originating in the wall of the gall-bladder. Graham does not doubt that such adhesions can cause definite symptoms.

I agree with Graham[467] that the mere separating of such pericholecystitic adhesions will do no appreciable good. Graham takes a stand which is quite commonly accepted, namely, that in such conditions the gall-bladder ought to be removed. I am quite sure that this would be advisable for the gall-bladders which, in addition to the pericholecystitic adhesions, show a marked pathology. But I am not so ready to accept cholecystectomy for pericholecystitic adhesions when the gall-bladder otherwise shows an apparently healthy status; there is considerable room for argument here. And it is not enough to say that a certain percentage of these cases get well after cholecystectomy; such a statement savors much of a hit and miss policy.

Non-surgical Biliary Drainage.[471-473] The case of Dunn and Connell[471] is worthy of record as a control observation because of the unique opportunity afforded for the elucidation of certain phenomena of biliary secretion with especial reference to the Lyon method.

A patient in whom a cholecystectomy had been performed subsequently developed attacks of pain and chills and fever, with vomiting and jaundice. After many vicissitudes and fourteen operations, a subject resulted in which there was no common bile duct, in which there were shrunken hepatic ducts, in which there was no gall-bladder, in which no anastomosis had been successfully accomplished between the hepatic duct and the duodenum, and in which there was an abdominal fistula that afforded direct access to the duodenal pool. For feeding purposes, a catheter led through this fistula into the duodenum. The patient's digestion was good and she felt well during the entire period in which the biliary studies were made; during part of this time she attended to her household duties.

It is obvious that such a combination of circumstances presents exceptional opportunities for study. Lyon's hypothesis is that under the action of a concentrated solution of bile placed in the duodenum a a sequential flow of bile is obtained: (1) A pale yellow ("A") bile which his hypothesis assumes comes from the common duct; (2) a darker, more viscid ("B") bile which is assumed to come from the gall-bladder; and (3) a clear yellow ("C") bile of low specific gravity assumed to be freshly secreted from the liver. On this hypothetic differentiation of bile flow, a scheme for the diagnosis and treatment of biliary tract lesions has been elaborated. Dunn and Connell have had an extraordinary opportunity for checking up all of these assumptions.

Dunn and Connell's[471] experiments suggest that one is dealing here with an intestinal absorption of the magnesium. In turn, they furnish the following alternative explanatory hypotheses: (1) An enterohepatic circulation of magnesium in which the latter, carried to the liver in the portal blood, acts directly on the liver as a cholagogue, producing a bile flow rich in pigment; or (2) a destruction of red blood cells, possibly by the magnesium ion, somewhere in the portal system, resulting in sudden dumping of an increased quantity of blood pigment on the liver, which reacts to this stimulus by an increased output of bile rich in pigment.

The adequately controlled experiments carried out on this patient have shown, further, that the assumption is not necessarily true that the B fraction of the A B C magnesium sulphate sequence represents gall-bladder bile, and that we are not yet justified in localizing disease of the biliary tract on evidence afforded by the Lyon-Meltzer method of bile segregation.

Friedenwald and Morrison[472] have employed the method clinically in 315 observations; the original plan of Lyon was followed. There were a variety of lesions represented in the series, but in only a number of these was the diagnosis verified by operation. One can summarize the observations as follows:

1. Cholelithiasis. In this disease little can be expected from this form of treatment as a curative measure. They believe, however, that following operation it is a means of overcoming infection and thus acts in a preventive way against the recurrence of symptoms. The objection that I find in the latter part of this is that after an efficiently done operation the method would be unnecessary.

2. Obstructive Jaundice. In catarrhal jaundice the results of Friedenwald and Morrison agree with those of Lyon. In the other varieties of obstruction there is an inability to obtain bile. This is explained either because of the obstructed duct (by stone, etc.), or by a bile which is too ropy and thick to flow. These observations seem to agree with those generally heard.

3. Chronic Cholecystitis. In this disease Friedenwald and Morrison obtained their best results.

4. Biliary Stasis. Lyon believes that so-called biliousness is really biliary stasis. Friedenwald and Morrison have obtained good results with daily treatments extending over many weeks.

Friedenwald and Morrison[472] conclude that while the method of treatment is still in its infancy, and is yet too new to enable one to draw conclusions, it nevertheless affords a means of relief in certain biliary affections. F. Neuhoff agrees with this opinion.

Cholecystectomy vs. Cholecystostomy.[474, 475] In general, the viewpoints of Moore[474] and of C. H. Mayo[475] reflect the best available opinions of the best surgical minds in preferring cholecystectomy to cholecystostomy and corroborate those reviewed in previous numbers of PROGRESSIVE MEDICINE. It is worthy of note that opposite opinions are most generally held by men of more limited experience, or those early in their surgical careers. It does not seem justifiable to make use of the results of such limited experience in making correct judgments as to the type of operation to be performed in gall-bladder disease. It seems more proper to make use of the experiences of men advanced in surgical knowledge and practise and when all of the published reports obtained under the latter conditions show a marked uniformity in preferring cholecystectomy to cholecystostomy as a routine operation, it seems idle to speak of the unsettled opinion in regard to the proper operation for gall-bladder disease.

In the ordinary form of *bile drainage after cholecystectomy*, Graham[467] chooses to pass a catheter through the stump of the cystic duct and thence into the duodenum. Such a procedure has several advantages. In the first place, the entrance is gained to the common duct with no trauma to that structure; the catheter passing through the sphincter at the ampulla causes the latter to relax and permits the continuous drainage of bile directly into the duodenum with a minimum of loss through the abdominal fistula. Reid,[479] of Baltimore, recommends a similar procedure even when an incision had been previously made into the common duct. The advantages outlined here, however, are more than counterbalanced by a distinct disadvantage. Many times drainage of bile is necessary for biliary conditions in which a subsequent precipitation of stones is highly probable, or when it becomes necessary to safeguard any deficiency of technic and the possible overlooking of small calculi; in the latter cases the technic must be so arranged as to permit the subsequent extrusion of any retained fragments. Under such conditions, drainage through the cystic duct, as indicated by Graham[467] and by Reid,[479] is insufficient. Deaver and other men recommend making, purposely, a large incision in the common duct.

I am impressed, however, with other advantages which Graham[167] speaks of; these are *the therapeutic possibilities of a tube in direct communication with the duodenum.* This has recently been pointed out by McWhorter and was first described by Starr, in 1899. The tube can be used to convey nourishment and fluids of various kinds into the intestinal tract; or, when the proper stage has been reached, for the introduction of cathartics. This has resulted, according to Graham, in a marked improvement in the postoperative convalescence.

Willis[476] contradicts the usually held impression that an *extravasation of bile* into the abdominal cavity is a danger to life. Such danger only exists when the extravasation reaches an enormous amount. He makes this a point in favor of the omission of drainage after cholecystectomy, as the indicated danger is the one which always creates the demand for drainage. A communication of C. H. Mayo[475] points out that drainage of the liver bed is what is needed. In a relatively "clean" case, both of these indications may be met by inserting a lead down to the area of operation. Whenever he is in doubt, Mayo satisfies his fears by leaving the double strand of catgut attached to the liver where the gall-bladder fundus was separated from it and continued in a suture down to the cystic duct. This catgut is brought out of the abdomen and the abdominal wall is sutured tightly around it. Should there be any indication within a few days of a retained secretion of any kind, forceps are passed along the strand of catgut into the abdomen as any drainage would have followed the catgut suture line to the abdominal wall. If, by the fourth day, the catgut is not required, it is placed under tension and cut beneath the skin.

I think that the method I am accustomed to use accomplishes the same purpose somewhat better. I insert one of the smallest-sized drainage tubes down to the stump of the cystic duct which, at the end of twenty-four hours, or, the latest, forty-eight hours, is withdrawn entirely. This establishes a tract in the event of any bile drainage and incidentally permits an immediate collapse of the drainage tract and its agglutination so that the wound heals promptly as if by primary union.

Transduodenal Choledochotomy. Simon[477] prefers to do transduodenal choledochotomy for stone in the terminal portions of the common bile duct rather than supra- or retroduodenal operations. He gives as one of the reasons for the preference, the inability to examine carefully the mouth of the pancreatic duct. I do not know how American opinion would generally correspond to this recommendation. I have the impression that most men would exhaust every other known method of operation for removing stones from the indicated position before they proceed to open the duodenum. It is difficult enough to make out the mouth of the pancreatic duct on the dissecting table; to do so during an operation would be most difficult and many times impossible.

Injury to the Bile Ducts and Methods of Repair. An excellent review of this subject is given by Sweetser.[486] Interference with the normal flow of bile into the alimentary canal is one of the serious accidents which may befall anyone because, if the normal flow be not reëstablished, the patient will more or less quickly die, and because the successful accom-

plishment of the proper return flow is extremely difficult and sometimes impossible. Such an accident may result from a stenosis of the ducts following a deep ulceration, from the obstruction produced by a tumor, from the constriction of the ducts produced by adhesions, or from the division of the common duct during the operation of cholecystectomy.

Such accidents are apparently not uncommon, and it is fair to assume that there must be many unreported cases, for none of us is prone to report his own disasters. It is, therefore, of extreme importance that all cases of attempted repair should be reported, the unsuccessful as well as the successful, so that a satisfactory and efficient technic may be developed for repair of injured biliary ducts.

The methods devised for these restoring operations have varied in order to meet the conditions encountered and because of their varied success. If the duct injury is immediately discovered, it is usually at once possible to approximate the divided ends of the duct successfully. Some of the cases, successful at first, have failed later, because of stenosis at the point of union.

In most of the cases, some time has elapsed since the production of the injury, and the ends of the duct have separated widely and lie buried in dense scar tissue. Under these conditions an end-to-end approximation is very rarely possible. Usually, some other means must be employed. The tissues which lend themselves best for a successful operation are those which normally are bathed in bile and consequently are immune to its irritative effect. Such tissues include the mucous membrane of the ducts themselves, and that of the stomach, duodenum or jejunum. When it is possible to approximate successfully these structures to the proximal end of the duct, the results have been permanent in the majority of cases. The failures have been due either to stenosis at the point of union, or to an ascending infection. To prevent this, in many cases, an attempt has been made to fashion a valve-like structure at the point of anastomosis. If there is even only a very small stump of the proximal duct, Sweetser, as well as other men, think it possible in almost every case to approximate either the stomach, duodenum, or jejunum to it.

In one general form of technic, a flap is used, fashioned from the wall of the stomach or duodenum, in order to construct from it a new duct. This duodenal operation has given better immediate and late results than any other method employed at the Mayo Clinic, and there it is looked upon as the operation of choice in the average case of this type. Even in the most hazardous cases in which jaundice has preëxisted for some time, with the resultant serious changes in the liver, the bloodvessels, and the blood, the permanent reëstablishment of biliary drainage by direct union of the hepatic duct and the duodenum can be accomplished with a reasonably low mortality. This method is also preferred by Simon.[477] In all of these cases the anastomosis is made easier if a temporary rubber tube is used as a splint to be discharged later through the bowel.

In a certain number of the cases this general type of operation is not possible. A number of substitute operations have been suggested, the

most successful of which includes the employment of a rubber tube to bridge the intervening gap, the exposed part of which is covered either by contiguous peritoneum or omentum. Attempts have also been made to bridge the gap by means of autogenous grafts, the tissues used including the appendix, pieces of fascia, and sections of veins. These attempts have invariably failed. The biliary fistulous tract itself has been used, or a loop of jejunum; both of these methods were unsuccessful. In a few cases the hiatus was at the liver surface, with no duct available for anastomosis; in these, a hepatostomy, or hepatenterostomy, has been done, but with meager success.

Carcinoma of the Common Bile Duct and Papilla.[489-491] For *carcinomatous stricture of the common bile duct*, Hotz[489] recommends the reconstruction operation of Herhoojen and Wilms. The site of the stricture having been delimited, the latter is liberated. The duct is opened below the constricted area. The structure is dilated and a small, rigid rubber tube is inserted, one end being threaded upward through the stricture into the hepatic duct and the other being pushed downward into the common duct toward the duodenum. The duct is then sutured over the tube. The buried drain remains in place permanently and drains the bile satisfactorily. Naturally, this is a palliative operation.

There are 44 *radical operations* recorded in the literature *for carcinoma of the common duct*. Twenty of these survived the operation, but only 1 of them (Korte's patient) remained free from recurrence for more than six years. These are very poor figures, but Palles[490] believes, nevertheless, that operation is justifiable under proper conditions because of the hopelessness of any other kind of treatment. In the major part of the duct, the operations are fairly simple. I reviewed the experimental work in regard to radical operations, when the growth involves the papilla, several years ago in PROGRESSIVE MEDICINE.

An ingenious method of applying *radium to a carcinoma of the papilla* is described by Abel.[491] A tube is passed into the stomach. Through the laparotomy wound the duodenum is exposed and opened. The radium in two tubes was anchored immediately against the growth; and the capsules containing the radium were attached to threads of heavy silk which, in turn, were fastened to the end of the stomach tube; the latter had been previously guided into the proper position into the duodenum. The wound was then closed. At the end of twelve hours, the capsules were readily withdrawn through the mouth by traction on the silk.

THE SPLEEN.[521-538]

Irradiation of the Spleen. Preliminary irradiation of the spleen to prevent hemorrhage at operation is recommended by Kurtzahn.[521] His experiments showed, however, that this measure did not prevent large hemorrhages but prevented the small parenchymatous bleedings; from the description given, it appears that the operation need not necessarily be limited to the spleen.

Ruptured Spleen.[522] From the location and anatomic relations of the spleen, it would seem that this organ is well protected from external

injury. Injuries are, however, relatively common. The literature contains the reports of Willis, Stubenrauch, Lilienfeld, Hagen, Johnson, Lotsch and Planson; the last have reported considerable numbers of cases. The reported mortalities of Lotsch (1908) and Planson (1909) averaged above 37 per cent. In the cases of *spontaneous ruptures* reported, one can usually find that some previous disease had preceded, such as typhoid, typhus or malaria. The question of the actual cause of the spontaneous rupture is still debatable; muscular action or over-distention are those usually considered. In late years, the results of operation have shown considerable improvement, and Connors[522] attributes these good results to the use of direct blood transfusion; I am much inclined to agree with Connors. Theis and Henschen and Hauke[524] recommend the reinfusion of the blood found in the peritoneal cavity.

While *splenectomy* is easily done with a mobile organ not held by adhesions, under the opposite conditions the difficulties may be many. In the latter, Lombard[560] decorticates the spleen. The plane of cleavage lies beneath the adhesions and between the capsule and the spleen tissue. By incising the capsule and inserting the fingers underneath it, the splenic tissue may be rapidly decorticated and freed. Previous ligation or compression of the pedicle between clamps allows easy completion of the operation. If the operation really works as well as described, it is a valuable addition to our operative methods.

It is rather astonishing to know that there are twenty-eight different methods of approach to the spleen. Ssoson-Jaroschewitsch[525] groups them as follows: (1) Simple laparotomy; (2) thoraco-laparotomy; (3) transdiaphragmatic laparotomy. The simple laparotomy incisions include vertical incisions through the rectus and oblique incisions at the border of the left costal arch, or combinations of the two; the latter include incisions with, or without, bending or resection of the costal arch. I take it that the truth of the matter is that no one incision is, perhaps, altogether satisfactory to every one and for all types of cases; and that, for practical purposes, it behooves one to make use of the simplest and then to school oneself thoroughly in its proper making and manipulation so that practise will make up for whatever deficiencies are inherent in the incision itself.

Enlargement of the Splenculus. Eccles[526] reports a case in which following a splenectomy the splenculus became enlarged and assumed the shape of a normal spleen. This, while a known phenomenon, is of extreme rarity insofar as its actual demonstration is concerned.

The résumé of Moynihan[528] on **the surgery of the spleen** is replete with useful information. The pathologic changes found in the spleen may be grouped best according to the affinities between the causative agent and the various parts of the spleen-liver system which they directly affect.

In the first type, the provocative agent excites either a mechanical effect or a local lesion of the exact kind produced in other organs. In the second type, an organism lodges firmly in the pulp of the spleen without actually producing a gross lesion. The best example of this condition is afforded by the chronic malarial spleen. The third type of

process is that which is set up by toxic processes reaching the spleen from some nidus elsewhere in the body. Especially in the examination of the dead body, foci are easily overlooked in the mucosa or submucosa of the alimentary canal in which there is no frank suppuration but merely a subacute inflammatory cell infiltration of slight or moderate extent.

The toxins which may enter or leave the spleen are grouped according to their supposed actions as follows: (1) The most active poisons which cause anemia; these prevent the formation of red blood cells; (2) the hemolyzing poisons which play the chief part in splenomegaly; (3) poisons which excite fibrosis; these are very common; (4) poisons. which excite cell proliferation; these may concern the cells of the Malpighian bodies as in lymphatic leukemia and some kinds of Hodgkin's disease or the cells of the spleen pulp.

Anemia may be caused by many diseases. When hemolysis is associated, the spleen is to be suspected, but fragility of the red cells does not necessarily indicate that the seat of the lesion is in the spleen. And every anemia with hemolysis does not result from a splenic disorder. The clinical phenomena of hemolysis are absent in those diseases in which the liver cells are competent; that is in Hodgkin's disease, myeloid and lymphatic leukemia, sarcoma of the spleen and lymphogranuloma.

When jaundice arises as a result of a toxic process in the spleen-liver system, consideration must be given to: (1) The site of action of the poison, and (2) the nature of the poison. The liver cells and their relation to splenic anemia and hemolytic splenomegaly are discussed by Moynihan who points out that the mechanism and interrelationships of the liver, spleen and pancreas are fairly complicated.

Instead of searching for this or that splenic disease, Moynihan[528] says that an inquiry should be directed toward the determination of the functional capacity of all of the various organs likely to be deranged. This derangement must be regarded not merely as a restriction of the morbid changes to the spleen, but as a disturbance of wide ramification throughout the whole body affecting one or other or, perhaps, even all of the form systems in which the spleen plays a part. It is possible that splenectomy in any of these diseases removes the obvious end-product of the morbid process and thus brings about a "cure" of the disease, or, perhaps, only an arrest of its development; but it does not, by any means, follow that all of the other related parts are thereby caused to return to their normal states. An absence of symptoms does not imply the restitution of normal function.

Modern therapy in splenic disease seeks to (1) stimulate the production of new blood by massive "step-ladder" transfusion of whole blood; (2) to overcome the absorption of hemolytic bacteria or their toxins by the radical removal of local foci of infection; (3) and to protect the newly formed and older red cells by removing the spleen.

The best American experience in regard to splenectomy for the various splenic disorders is that of the Mayo Clinic.[529–534] The tables which are herewith reproduced from Giffin's[529] paper give this information in the most concise way, are self-explanatory and give a very good idea of present-day possibilities.

TABLE I.[529]—SPLENECTOMY TO SEPTEMBER 20, 1920.

	Cases.
Splenic anemia	71
Septic splenomegaly	10
Hemolytic jaundice	32
Pernicious anemia	53
Myelogenous leukemia	26
Portal cirrhosis	10
Biliary cirrhosis	6
Luetic splenomegaly	6
Lymphocytic splenomegaly	6
Gaucher's disease	4
Tuberculosis of the spleen	4
Wandering spleen	2
Hodgkin's disease	1
Eosinophilia with splenomegaly	1
Neutrophilia with splenomegaly	1
Local bleeding at operation	1
Miscellaneous, questionable diagnosis	11
Total	245

TABLE II.[529]—HOSPITAL MORTALITY IN THE LARGER GROUPS OF
SPLENECTOMIZED PATIENTS.

	Cases.	Deaths.	Per cent.
Splenic anemia	71	9	12.6
Hemolytic jaundice	32	1	3.1
Pernicious anemia	53	3	5.6
Myelogenous leukemia	26	1	3.8

TABLE III.[529]—SPLENIC ANEMIA.

Cases to September 20, 1920	71
Hospital deaths (12.6 per cent)	9
Subsequent deaths	22
Patients heard from	28
In good condition	22
In fair condition	5
In poor condition	1
Patients operated on five years or more	27
Patients who lived more than five years	17
Still living	16

Note: One patient is well eleven years and five months after operation

TABLE IV.[529]—SEPTIC SPLENOMEGALY.

Cases to September 20, 1920	10
Hospital deaths (20 per cent)	2
Subsequent deaths	5
Patients living	3
In good condition	1
In fair condition	2

TABLE V.[529]—HEMOLYTIC JAUNDICE.

Cases to September 20, 1920	32
Hospital deaths (3.1 per cent)	1
Subsequent deaths	3
Patients heard from	26
In good condition	22
In fair condition	4

One patient is well nine years after operation.

TABLE VI.[529]—PERNICIOUS ANEMIA.

Cases to September 20, 1920 53
Hospital deaths (5.6 per cent) 3
Subsequent deaths 43
Patients living 7
Eleven patients lived more than three years after operation, 5 are still living between four and five years after operation.

TABLE VII.[529]—MYELOGENOUS LEUKEMIA.

Cases to September 20, 1920 26
Hospital deaths (3.8 per cent) 1
Subsequent deaths 15
Patients heard from 7
   In good condition 5
   In poor condition 2
One patient died five years four and a half months after operations; 7 patients lived more than three years after operation, six of these are still alive.

TABLE VIII.[529]—SPLENECTOMY—MISCELLANEOUS.

Diagnosis.	Cases.	Hospital deaths.	Subsequent deaths.	Deaths.	Remarks.
Gaucher's disease .	4	1	1	One more than three years after operation	No report from 1; 1 in good condition more than twelve years after operation.
Wandering spleen .	2	0	0	. . . .	One in fair condition more than seven years after operation and 1 in good condition more than twelve years after operation.
Splenomegaly with eosinophilia	1	0	1	More than four years after operation	
Splenomegaly with neutrophilia . .	1	1			
Local bleeding at operation . . .	1	0	1	Less than one year after operation	
Hodgkin's disease .	1	0	1	Less than one year after operation	
Miscellaneous questionable . . .	11	2	5	Four less than one year and 1 less than two years after operation	No report from 1; 1 in good condition less than one year and 1 less than two years; 1 in fair condition less than five years after operation.

Cysts of the Spleen. The literature of the surgical pathology of cysts of the spleen includes contributions by Aschoff, Beneke, Boettcher, Coenen, Fink, Otto, Renggli, Ramdhor, Schmidt, Heinricus, Monnier and Lasperes. The first American papers are those of Bryan (1905) and of Powers (1906). There are two contributions this year, one by Fowler,[537] and the other by Hamilton and Boyer.[536]

Splenic cysts may be classified as follows:

1. Parasitic cysts.

2. Dermoid cysts. There are only 2 authentic cases on record 1 of Andral and 1 of Kummaris.

3. Non-parasitic cysts. Fowler's classification of the cases in this group is the following:

A. True cysts. There are a number of sub-groups:

(a) Infoliation cysts. These include inclusions of peritoneum and inflammatory or traumatic cysts. They may be small and multiple and may be superficial or deep.

(*b*) Dilatation cysts. These include polycystic disease of the spleen (Coenen, Fowler) explained on the basis of an ectasis of the splenic sinuses.

(*c*) Neoplastic types (lymph- or hemangioma). There may be difficulties in distinguishing between group *b* and *c*.

B. Pseudocysts. These may arise in the midst of an old hematoma and are usually large and unilocular. Hamilton and Boyer's[536] 2 cases probably belong in this group. Psudocysts may also arise as degenerative phenomena arising from secondary changes in infarcted areas; these, too, are usually large and solitary.

Small cysts seldom cause any symptoms. The larger cysts give rise to symptoms by pressure and traction. The diagnosis may be made by one or more of the following procedures. (1) The finding of a fluctuating tumor definitely associated with the spleen; (2) by aspiration; (3) sometimes nothing by an exploratory incision will reveal the true nature of the lesion.

Bircher gives the following results of operation:

1. Puncture by cautery	. . . . .	6 cases	2 deaths
2. Incision and drainage	. . . . .	9 "	1 death (by sepsis)
3. Resection of the cyst	. . . . .	4 "	1 "
4. Splenectomy	. . . .	15 "	0 deaths

Fowler's[537] series of 23 splenectomies up to 1908 had a mortality of about 17 per cent. One of the difficulties he points out is that in about four-fifths of the cases the liver or some other organ is involved.

W. J. Mayo[532, 533] interprets the figures regarding the cases of *pernicious anemia* as indicating that in at least one-third of the cases the average life of the patient has been considerably prolonged, and that in about 10 per cent the prolongation is sufficient to lead to the hope that a cure may result in some cases; this in spite of the fact that it has been a tradition in the medical profession that recovery of a patient in the face of the diagnosis of pernicious anemia proves the diagnosis wrong. This conviction is still very strong. In the average case the palliation following splenectomy has been much greater than that produced by blood transfusion. In a general way, following splenectomy, the course of the disease seems to be ameliorated, the relapses are less frequent and severe, and the cord changes less rapid. The removal of the spleen terminates the abnormal destruction of red cells but does not greatly affect the disease otherwise. When the disease has advanced to a point at which the bone marrow has been injured beyond the power of recuperation, the most that can be expected from treatment is a temporary abatement of the symptoms. The question has not yet been answered whether pernicious anemia is a definite entity, or whether it is the end-result of several conditions and recognizable as pernicious anemia only when the patient has reached the state which we know will eventuate in death.

THE PANCREAS.[502-529]

The Complete Removal of the Pancreatic Gland in animals is usually followed by death. The report of Chand's[502] patient is therefore of

interest. The patient had a large cyst of the pancreas the removal of which necessitated the extirpation of the entire organ. At the present writing—more than two years later—the patient is apparently in good health and there is no diabetes. Success under these circumstances should be interpreted in the light of Horgan's observations—which have been known for some time—that additional pancreatic tissue is very often present in the alimentary canal. Then, too, it is always possible that the entire pancreas had not been removed.

Deaver[507] points out that the pancreas is so often involved in pathologic conditions of the viscera surrounding it and even in disease of more remote regions, and direct attack on the organ is still so fraught with danger, that a proper consideration of disease which precedes or causes acute or chronic pancreatitis is of vital importance. It is quite common knowledge that the most frequent forerunner of pancreatic disease is some affection of the biliary tract. I wish to allude, however, to the fact that frequently the base of an ulcer, either of the stomach or of the duodenum, lies in intimate contact with the lobules of the gland and so forms a direct potentiality for infection of the pancreatic gland. While cases of this type are common, hitherto, the elicitable symptoms have been referred to the ulcer. It is open to question, however, whether some of the symptoms, both before and after operation, have not some relation to the pancreatic involvement.

Peice[509] reports a case in which, after resection of the duodenum for ulcer, an acute suppurative pancreatitis developed, with multiple foci of necrosis in the subcutaneous adipose tissue. The patient finally recovered after a number of operations. This is the second case of complicating pancreatitis after a duodenal operation and is one of the few cases on record of subcutaneous fat necrosis with acute pancreatitis.

Pancreatic Cysts.[512, 515, 516] A number of cases of pancreatic cyst are reported this year together with a short résumé. In Ballin and Saltzstein's[512] case there was a clinical complex in which cholelithiasis, cholecystitis and pancreatitis could be recognized; this bears out Deaver's contention as to the mechanism of pancreatitis. Following a cholecystectomy, a pancreatic cyst developed; the actual mechanism for the formation of the latter included a severe pancreatitis which was followed by some interference with the biliary outflow and an accentuation of the pancreatic condition with breaking down of the pancreatic tissue. Leakage into the peritoneal cavity resulted in cyst formation.

This seems to be the generally accepted opinion: namely, that true pancreatic cysts follow a chronic pancreatitis in which scar formation obstructs the ducts. Other causes include (1) simple or malignant proliferation cysts; (2) congenital cystic disease similar to polycystic disease of the kidneys—this is very rare—; (3) hydatid cysts (also rare); (4) pseudocysts. The last are collections of fluid in close proximity to or in direct connection with the pancreas. These are usually due to traumatism but may result from acute hemorrhagic disease of the pancreas with rupture of the organ.

In many of the cases it is difficult for the operator to locate the cysts with relation to the surrounding structures and to determine whether

they are true pancreatic cysts or pseudocysts. The exact nature of the true cyst cannot be determined in many cases for a number of different reasons.

Pancreatic cysts affect both sexes about equally between the thirtieth and fiftieth years. Trauma seems to be rather an uncommon cause; both Steindl and Maydl[513] and Judd[516] each mention only 1 case, although there are about 267 cases in the literature. The presence of these cysts is characterized by pain in the upper abdomen usually caused by pressure upon the surrounding viscera or upon the diaphragm or celiac plexus (Steindl and Maydl[513]), by vomiting and by the presence of a palpable tumor. Aspiration is to be condemned; x-ray studies and laboratory data are of secondary importance only. Glycosuria and fatty stools are never observed (Steindl and Maydl[513]). A positive diagnosis is possible in about one-half of the cases.

The fluid content of a pancreatic cyst is light colored and viscid, or more often, dark because of the presence of blood. One clinical characteristic is the power to corrode the skin when the fluid escapes into the abdominal wall.

Enucleation is the ideal form of treatment but is frequently impossible because of technical reasons; marsupialization then becomes the operation of necessity.

Carcinoma of the Pancreas. The spread of carcinoma of the pancreas was studied by Adams.[517] The features which he emphasizes are (1) the tendency of these tumors to invade the blood stream locally; and (2) the occurrence of generalized carcinomatosis by blood dissemination. Metastatic foci in the suprarenals are common. Carcinoma of the pancreas is also prone to ulcerate into the intestinal tract. In 11 cases observed by Adler,[519] the relative frequency of involvement was the following: Stomach, 2 times; duodenum, 4 times; gall-bladder, once; colon, 4 times.

THE SUPRARENALS.[538-546]

Aplasia of the Suprarenal Glands. Schnyder[538] makes the point that when an aplasia of one suprarenal gland develops (usually this involves the right one) the other gland frequently becomes the seat of a tuberculous infection with the development of the picture of Addison's disease.

Extirpation of the Suprarenal Glands in the Treatment of Epilepsy. Influenced by Fischer's theory that by the reduction of suprarenal substance the tendency to convulsive seizures is lessened, Brüning[542] has removed the left gland in 9 cases of epilepsy. The experiment was not successful in every particular, but an improvement was effected in all cases which, in some, practically amounted to a cure. Two of the patients were entirely freed from attacks. The cases that were unsuccessful were, perhaps, not carefully selected because of lack of experience. Brüning does not wish to be understood as claiming that all cases of epilepsy can be cured in this manner. He simply regards the operation as pointing to a new method which will make it possible, in a certain number of the cases, to relieve in a measure the main symptoms of epilepsy, the convulsions.

Peiper[541] followed Brüning's method in 7 cases. He had immediate good results but, unfortunately, recurrences soon set in. Peiper's experience is, of course, discouraging. Bumke[540] and Kuttner apparently have also done this operation; they recommend a slightly different technic than that of Brüning.

Malignant Suprarenal Tumors. Orthmann[543] analyzed 147 operative, and 140 postmortem cases of malignant tumor of the suprarenal glands. Of the total, 66 were carcinomata, 55 sarcomata, and 115 hypernephromata. Male subjects predominated; and the ages ranged from sixteen to eighty-nine years.

Curtis and Potel's[544] case of suprarenal tumor of the abdominal wall is interesting because it suggests that certain hemorrhagic lipomas of the abdominal wall may, in reality, be types derived from aberrant suprarenal tissue.

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GYNECOLOGY.

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CANCER OF THE UTERUS.

The Cancer Problem. Another year has rolled by, and although we still must confess that cancer has not been conquered, nevertheless we feel that we are gradually nearing our goal, however far away that goal may be. The many enthusiastic reports concerning radiotherapy in cancer of the female pelvic organs, the lively discussion about radium at the Philadelphia meeting of the American College of Surgeons following Deaver's pessimistic remarks and the large amount of radium which has been purchased by both public and private funds during the past year all point out that the subject of cancer and its treatment has not been in a hibernating stage, but, on the contrary, has been receiving an unusual amount of attention. We shall go into more detail when we consider the subject of radiotherapy, but at the present time we must confine ourselves to the problem of cancer control.

One of the most earnest students in this country, perhaps in the world, of the subject of cancer control, especially from the statistical standpoint, is Frederick L. Hoffman, whose book on the subject of cancer statistics, which we have reviewed in a previous volume, is a masterpiece, of which he may well be proud. In a more recent article he[1] states that the cancer problem is as baffling today, if not more so, than it has ever been. The subject is becoming more ramified as research in one direction or another proceeds and as new problems arise, or new discoveries are made. No one can today lay claim to a thorough grasp of the whole subject further than in broad outline, and even that is a task of considerable difficulty. When the Society for the Control of Cancer was formed, it was clearly realized that the main objective of its propaganda should be to arouse the general public to the menace of cancer increase and the hopeful effects of early diagnosis and surgical treatment in the early stages of the disease. It was for this reason decided not to call the society one for the prevention, but rather for the control, of cancer. In other words, the aim of the society is to bring about a reduction in the death rate from cancer as the results of early methods of treatment, whether surgical or otherwise. Nothing of value is known at the present time that would justify the belief that cancerous processes can be prevented: but the knowledge of precancerous conditions leads to earlier diagnosis and treatment at a stage when the prognosis is generally quite favorable. Regardless of what the Society has done, and it has done much, there has not as yet been a marked effect on the cancer death rate. In some

[1] Minnesota Medicine, 1921, **4**, 124.

localities where the campaign has been most effective, the rate has unquestionably declined, on account of cases coming earlier to operation. But, in a general way, it may be said that the vast majority of cancer operations still take place when the disease has reached an inoperable condition. Cancer is not only one of the most important causes of death, but the disease is increasing from year to year in practically all civilized countries.

In the continental United States it may be conservatively estimated that during the past year there were not less than about 90,000 deaths from malignant disease. On the basis of an earlier estimate, the approximate number of deaths from cancer is divided somewhat as follows: Stomach and liver, 32,000; female generative organs, 12,500; peritoneum, intestine and rectum, 11,000; female breast, 8500; cancer of skin, 3500; cancer of the buccal cavity, 3500; and of other organs or parts, 13,000, a total of 84,000. This statement illustrates the wide diversity of the cancer problem and emphasizes the importance of considering the cancer question in detail, rather than in general terms, for methods of treatment applicable to one form of cancer may be wholly inapplicable, or partly so, to another form. The statement also illustrates the great importance of accurate death certification. It is lamentable that so many certificates should be sent in containing merely the term "cancer." It is obviously of the first importance that the organ or part of the body affected should be stated for it will not advance the cause of cancer control to deal with statistics limited to cancer mortality in general terms. It, no doubt, entails a certain amount of additional labor on the part of the doctor to fill out a certificate in detail, but by doing so, much subsequent and more burdensome correspondence is avoided. The cancer death rate in the continental United States has been increasing from year to year, at the rate of about 2.5 per cent per annum. There is no corresponding increase in the death rate of any other disease or group of diseases, and considering the vast amount of useful knowledge concerning the cancer problem, the increase reflects a lamentable apathy on the part of both the public and the medical profession toward the problem of the earliest qualified diagnosis, followed by the earliest radical method of treatment. Since the propaganda for cancer control is largely limited to cities or urban communities, it will be of interest to point out that the cancer death rate of twenty representative American cities increased from a rate of 72 per 100,000 in 1904 to 89 per 100,000 in 1914 and to 94 per 100,000 in 1918. Hoffman insists that this increase in real and not apparent. In fact, he states that the true increase in cancer liability is much greater, for operative interference has in the meantime increased materially in efficiency. If it were possible to ascertain the number of successful cancer operations during the course of a year and, by means of a follow-up system, the number of successful cures within a given period of time, it would become clearly apparent that the liability to cancerous affections is possibly today 50 per cent greater than it was fifteen years ago. The control of the cancer death rate is primarily a surgical question for unless the offending mass of cancerous growth is promptly removed in

the early stage of the disease, death is a foregone conclusion. Hoffman directs our attention to the fact that the negative side of the cancer question is as important as the positive side. It is as urgent that we know or understand why cancer does not occur in certain races or in certain sections, as why the rate should be one of extraordinary and exceptional frequency. Cancer, for instance, practically never occurs among our native Indian tribes and another most significant phase of the problem, also generally ignored by those who should give consideration to the question is the very rare occurrence of cancer of the female breast among the Japanese.

Considering the question of heredity, the conclusions derived from animal experimentation are diametrically opposed to the facts, as far as known, for the human race. Cancer is certainly not inherited in human beings in the same sense as the hereditary predisposition is frequently apparent in tuberculosis. Cancer is now so common a disease of adult life that the occurrence of cancer cases in more than one individual of the same family may be looked upon as a true coincidence. The cases of exceptional frequency sometimes reported, even granting the absolute accuracy of the facts, are in the nature of abnormalities, with only a slight bearing on the practical side of the question. There are no reasons why a cancerous predisposition should not be inherited, or, in other words, why persons living the same kind of lives in the same kind of environment, subject to about the same external influences, should not suffer likewise from cancerous affections, but no statistical evidence is available to prove that cancer is inherited in the accepted sense of the term, all the experiments on rats, mice and guinea-pigs notwithstanding. Much is said of cancer villages and cancer houses, but all investigations by qualified experts have shown the fallacy of the assumption other than as previously observed, that the general environment, topographic features or perhaps the occupational pursuits may predispose to an excessive rate of cancer frequency. Occupational cancers are a fact and not a theory. Chimney-sweep's cancer is unquestionably a direct result of soot irritation, just as x-ray dermatitis is a direct result of x-ray exposure. Here also an extended discussion would be necessary to illustrate the problem from a practical point of view. X-ray dermatitis however, may be referred to as evidence of external conditions, within our knowledge and understanding, acting as causative factors in malignant disease and there are no reasons for supposing that the true causative processes vary extensively in other forms of cancer than in occupational skin disease. An important phase of the cancer problem is the higher rate of frequency of cancer of the uterus among married than among single women. Investigation has also brought out the fact that cancer of the breast is relatively more frequent among the unmarried and the same holds true of malignant ovarian tumors.

Finally, Hoffman refers to the apparent difference in cancer occurrence according to economic status. There seems to be no serious question of doubt that cancer is more frequent among the well-to-do than among the poor, and since prosperity is practically the equivalent of hyper-

nutrition, the conclusion seems justified that overnutrition is a pre-
disposing factor of considerable importance. It is true that there is a
divergence of opinion on this question but Hoffman's investigations
conclusively proved to him that cancer is more common among persons
of overweight than those whose weight falls below the normal standard.
Since poverty and undernutrition, or malnutrition, go practically
together, there is here another neglected field where specialized research
gives promise of useful results.

Experimental Cancer Production has occupied the attention of labora-
tory investigators for the past twenty years and the sum total of our
present knowledge along this line is well and so briefly described in an
editorial of the *Journal of the American Medical Association* (1921,
lxxvi, 1404) that we shall transcribe it practically *in toto*. Experimental
work of this type, this article points out, received its initial stimulus
from the independent observations by Leo Loeb in this country and by
Jensen in Denmark, that spontaneous tumors arising in rats and mice,
may, at least under certain conditions, be transplanted from animal to
animal in series. Investigation of such transplanted tumors has engaged
students of cancer ever since that time, and much has been learned con-
cerning the biology of the cancer cell by this means. Less positive
information than was expected has been obtained concerning the
etiology of cancer. Most of the evidence furnished by study of trans-
planted mammalian cancers has been interpreted as indicating that
they probably are not the result of infection produced by some specific
cancer parasite, whereas the transplantable, sarcoma-like growths of
fowls, found by Peyton Rous to be transmissable by cell-free filtrates,
suggests the existence of just such specific cancer parasites. A funda-
mental limitation of the usefulness of the transplanted tumors as a
source of information lies in the fact that they are far from being identical
with spontaneous tumors. They merely represent artificially produced
metastases of the tumor of one animal into the tissues of another, and
are always growths of cells derived from the cells of the original tumor
animal and not the cells of the host. The spontaneous tumor, of course,
represents growth of the tissues of the animal that bears it. The
inoculated animal, in all probability, would never have had a tumor of
its own tissues. Hence the conditions must be quite different from
what they are in the animal that suffers malignant transformation of its
own tissues. As evidence that there is such an essential difference, a
large proportion of implanted tumors may undergo spontaneous dis-
appearance and cure, which apparently never happens with spontaneous
malignant tumors.

Of late, more and more attention has been given to the experimental
production in animals of spontaneous tumors, which presumably will
give more useful information, especially concerning questions of etiology.
Several apparent successes have been registered which stimulate further
study and promise valuable additions to our knowledge to this baffling
problem. So far, the successful experiments have been attained in two
ways: either by imitating conditions that are known to produce cancer
in man, or by taking advantage of conditions that produce cancer in

animals. In the first group comes the production of tumors by long-continued stimulation of tissues by chemical or physical agents. Among these, perhaps the most striking results have been obtained by Japanese investigators. Applying the recognized fact that cutaneous cancers occur with particular frequency in those exposed to tar, Yamagiwa and his associates painted coal tar on the inner surface of the ears of rabbits every two or three days for long periods, with the result that great overgrowth of epithelium was produced which sometimes manifested all the histologic and clinical features of malignant cutaneous cancer, even to the production of metastases in the regional lymph glands. These positive results have particular significance from the fact that spontaneous skin cancers have never been observed before to arise on the ears of rabbits, and hence coincidence is out of the question as an explanation for these growths. More recently, Tsutsui has produced cancer in the skin of mice by the same means. Coal tar was painted frequently on the back of 259 mice, of which only 67 lived more than one hundred days, 16 developing carcinoma and 1 a sarcoma. As 2 of the epithelial growths produced lung metastases, the true cancerous nature of at least some of the growths is certain, although proper objection to too ready acceptance of epithelial infiltration alone as sufficient evidence of true malignancy has been raised, especially by Bullock and Rohdenburg. The latter danger is particularly shown by the infiltrative growths of epithelium that are produced by the injection of fat-soluble dyes, such as scarlet red, which often resembles the histologic picture of carcinoma almost perfectly, yet they disappear spontaneously when the exciting agent is removed or exhausted. Despite the extensive epithelial growths produced by fat dyes, the production of true carcinoma by this agent seems not yet to have been accomplished in a conclusive manner. Even repeated injections of scarlet red oil into the mammary gland of rabbits by Takeuchi did not produce carcinoma. A possible exception is furnished by Yamagiwa and Ohno who injected scarlet red oil into the uterine walls of 41 fowls and obtained 3 with adenocarcinoma. Here the uncertainty lies in the fact that abdominal carcinoma is occasionally observed to arise naturally in fowls. However, since continued mild stimulation of cell growth seems to furnish the most favorable means for inciting cancer formation, it seems probable that such proliferations as result from the fat dyes may develop into true cancer when other circumstances are favorable. As analogy, we have the well-established influence of the irritation of the bladder by anilin or its compounds in dye workers in the production of "dye workers' cancer."

The first striking successful attempt to produce tumors experimentally, by reproducing the conditions in which they have been found to arise in animals, was reported by Fibiger. Observing that cancer of the stomach occurred frequently in the stomach in rats that had eaten roaches infected with a parasite, he fed rats such infected material purposely and obtained a certain number of animals with what seemed to be true carcinomas resulting from the irritation caused by the parasites in the stomach. More recently there has been reported from the

George Crocker Research Fund at Columbia University the occurrence of growths in livers of rats infected with tape worms, the hepatic cysts stimulating the formation in the tissues about them of neoplasms that have all the characteristics of sarcoma. Since these growths develop in a much larger proportion of infected animals than in the case of Fibiger's spiroptera-infected rats, they may be correspondingly more useful in the study of cancer but suffer the disadvantage of being sarcoma rather than carcinoma. Another method of producing spontaneous tumors in mice seems to be established by the studies of Maud Slye on the influence of heredity on the incidence of tumors in mice. According to Slye's more recent observations, it is possible not only to produce stocks of mice with a high and fairly constant incidence of tumors, but even to obtain strains of mice with a tendency to produce certain types of tumors, as sarcoma, or tumors of certain organs, such as liver tumors, lung tumors, and mammary gland tumors. While the method of selective breeding seems able to produce an abundance of tumors and a choice of type or location of the growth, it involves too many years of breeding and selection to make it readily available at present, although it is possible that in the future it may find wider adoption as a means of producing stocks of animals with a high calculable incidence of spontaneous tumors of different site and type. It is to be noted that none of these methods of production of spontaneous tumors depend on the existence of any form of specific cancer parasite. Either inheritance, or the chronic stimulation of cell growth by mild irritation, or the co-operation of both factors, seem to be the determining influences. On the other hand, we are still a long way from finding an agent or method that will produce a cancer in every animal to which it is applied.

Organism Associated with Transplantable Carcinoma. Nuzum[1] has made an intensive study of a transplantable carcinoma known as the Croker carcinoma No. 11. This investigation has extended over a period of more than two years, involving several hundred cultivation experiments with cancer tissue in the special tissue ascitic fluid media. More than 1200 white mice were inoculated with cultures and tumor tissue. The investigation has been entirely limited to the same mouse tumor received on four different occasions from the Crocker Research Fund. Employing the special tissue ascitic fluid media under partial anaërobic conditions, a minute, filtrable, Gram-positive micrococcus has been isolated quite constantly from emulsions or pieces of carcinoma tissue removed under sterile precautions. The minute coccal bodies present some difficulty in isolation in the original cultures but transfers to subculture generations gradually effect a more rapid and luxuriant growth once the organism becomes adapted to artificial cultivation. It has been carried to the twelfth subculture generation under anaërobic conditions. The minute microörganism has been seen in stained sections of early carcinoma produced by trocar inoculation of tissue grafts in the usual manner. It has been frequently demonstrated in contact smears of carcinoma cells stained by Gram's method. It has never

[1] Surgery, Gynecology and Obstetrics, 1921, **33**, 167.

been encountered in the many control tubes of culture media incubated simultaneously with the cultures. The organism is present so constantly in this transplantable carcinoma of the mouse that one may or may not be justified in assuming that it plays some important role in the propagation of this tumor. One might assume that the minute coccal bodies invade the cancer cell and are carried along with them acting possibly as a continual irritant to the cell nuclei resulting in limitless division and multiplication. If this assumption is correct, we must conceive of two factors or agents responsible for the growth of this mouse tumor, the cancer cell itself and the minute microörganism present within the cell.

Injections of pure cultures of the organisms subcutaneously in the breast tissues of mice have in many instances reproduced tumor nodules which grow progressively for periods of ten to thirty days and slowly regress in the majority of cases. Microscopic sections of such tumor nodules removed at twenty-four hour periods reveal a mass of newly formed tissue cells rapidly dividing and supported by a newly formed stroma which becomes vascularized. By stimulating the tumor cells to their maximal degree of virulence either by incomplete surgical removal with recurrence of the tumor followed by rapid passage through a series of mice of the same stock or, by injecting cultures of the organism into grown tumors followed by transplantation, a method has been found whereby pure cultures of the organism have reproduced newgrowth. Subcutaneous injections of anaërobic cultures of the minute organism under these favorable experimental conditions designed to exclude the probability of carrying over lung cancer cells, have in several isolated instances lead to the production of tumors which grew steadily producing cachexia of the mouse. Histological studies have shown that these tumors do not vary in structure from the original growth known as the Crocker carcinoma No. 11. Transplants from the tumor growth produced by injections of the organism have yielded similar growths in 80 per cent of a series of inoculated mice. The organism has been readily recovered from these experimental tumors. Inoculation of cultures into and adjacent to tumors appear to stimulate the growths and enhance the virulence of the tumor tissue in subsequent transplantations.

In contrast to these observations, control injections of a limited number of cultures of staphylococcus aureus and albus, bacillus prodigiosus, and streptococcus hemolyticus into normal mice have never in Nuzum's experience reproduced tumor growth; abscess formation or septicemia being the usual result. Furthermore, when active cancer cells are mixed with cultures of ordinary bacteria, inoculations in mice usually fail to give a "take." Finally, it should be clearly stated that Nuzum makes no claim of having discovered the cause of cancer. The association of minute organisms with the cancer cells of the transplantable mouse carcinoma suggests that further careful study be made of this organism. While it is theoretically possible that living cancer cells may have been carried along in subcultures, the observations recorded suggest that two agents may be concerned in the etiology of this mouse carcinoma; the first agent being the minute coccal bodies

stimulating the cells to rapid division, and second, the cancer cell itself closely associated with the organism and transmitting it from host to host in subsequent transplantation.

Radiotherapy. During the past year radium has come into the limelight more than ever before as a result of several unusual occurrences. In the first place, the visit of Madam Curie, the discoverer of radium, to this country managed to create considerable newspaper publicity concerning both the woman and the element. It is generally well known how well she was received throughout the country and it was a wonderful tribute to her work and her personality when President Harding presented her with one gram of radium, the gift of the women of the United States in appreciation of her marvelous work. Those of us who had the pleasure of seeing and hearing Madam Curie during her visit could not help but be impressed with the sincerity and modesty of this frail little woman, who, through her tedious work leading to the well known discovery, unconsciously probably did more for the cancer patients than any woman who ever lived.

Another event of general interest, especially in the vicinity of Philadelphia, occurred about the end of November of last year, when the City of Philadelphia opened the first municipal radium clinic in the United States. It is true, as we recorded in a previous contribution, that the State of New York purchased two and one-fourth grams of radium for the treatment of the public without charge, but to Philadelphia must go the credit of being the first city to spend upwards of $150,000 for the purchase of two grams of radium which is to be for the treatment of any patient applying whether or not payment can be made. The plant constructed at the Philadelphia Hospital, where the radium is kept, is deemed one of the best equipped in the country. Of course, the element itself will not be used, but the emanations will be collected and applied to patients, of whom eighty a day can be accommodated.

The foregoing incidents caused quite a bit of comment by the lay press and in turn by the laity as a whole, but "the shot that was heard 'round the world," both by the medical profession as well as the laity, was fired when Deaver delivered his presidential address before the American College of Surgeons at the annual meeting of that organization in Philadelphia on October 24, 1921. In order not to misrepresent Deaver,[1] as may have been done by the lay press, let us quote directly from his address as published: "Men of experience have seen method after method heralded as a panacea, lauded to the sky, only to fall in disuse and be consigned to a well deserved oblivion, because it has failed to stand the acid test of experience. I hesitate to express my fear that this may prove to be the ultimate fate of radium treatment for cancer, for I should greatly regret to see our fervent hopes rudely shattered. But at least I feel justified in sounding a note of warning against too great expectations, for we have already found that it falls far short of being a universal cure and, indeed, in many situations where we most need help, it has proved sadly lacking."

[1] Surgery, Gynecology and Obstetrics, 1921, **33**, 605.

Exactly what Deaver intended to convey to his audience we shall not attempt to explain, but it is extremely unfortunate that his remarks found their way into the daily papers throughout the country and thus were read by millions of people who are in the habit of implicitly believing any scientific or pseudo-scientific information contained in the newspapers.

Needless to state, there were many surgeons throughout the country who were ready to answer and refute Deaver's remarks, and it may be of interest at this time to quote the opinions of some of our best men as expressed at that time. Thus, Francis Carter Wood, Director of the Institute of Cancer Research at Columbia University, in an interview published in the *New York World*, October 26, 1921, says, "Dr. John B. Deaver, in discussing the failure of radium to cure cancer, speaks as a general surgeon and not as a specialist. He believes, as does the medical profession in general, that at the present time radium will not cure internal malignant tumors, especially those of the stomach and intestine, even though it may greatly relieve them or retard their growth. What radium will do in the future it is impossible to say: but there is no reason to believe that it will cure all kinds of cancer. Indeed, some types are so very resistant to this interesting physical agent that the destruction of the cancer cells requires such large doses that the surrounding healthy tissue is more damaged than are the diseased structures. On the other hand, it is well known that radium is extremely effective in curing the small cancers of the face, which are, fortunately, much less malignant than those in other parts of the body, and it is quite justifiable, contrary to Dr. Deaver's statement, to use radium on such tumors if their exact nature is known. There are many instances of cures of such face cancers, the patient having remained well for ten to fifteen years after the treatment. In cancer of the womb, also, radium has been most valuable. Whether it will be found to cure permanently cancer of this region we are not prepared to say, but that the palliative results are often extraordinary is generally acknowledged. Women are not infrequently restored to full health even for a year or two, and entirely relieved of pain and discomfort and are able to go back to their regular household duties. While such improvement is often only temporary, wider experience in the use of large quantities of radium may ultimately make possible the attainment of a certain number of permanent cures in patients whose cancer is so extensive that they cannot be operated upon. When the cancer of the womb is very small and localized, surgery is to be preferred, but when the results of surgery are doubtful owing to the wide extension of the growth, radium is the better. Dr. Deaver's statement that he hesitates to express the fear he has that nothing can be looked for from radium in the future, is a very unsafe generalization. In the last three years we have learned more about the use of radium and x-rays than we learned in ten or fifteen years before. There is no question that in a few instances most extraordinary results have been obtained. To say that there is going to be no more progress in the future is to be far more venturesome than I am willing to be. No one can say what the future will bring forth."

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Dr. Harvey Gaylord, Director of the New York State Institute for the Study of Malignant Disease at Buffalo, in commenting upon Dr. Deaver's statement, says in an interview in the *New York World*, October 27, 1921, "Such an utterance smacks of the surgical knowledge of the middle ages. This is no time to raise the question whether or not radium is more efficacious than surgery in the treatment of cancer. Radium has cured cases of cancer which the surgeons could not help. In other cases, far advanced, radiation has lengthened life, relieved suffering and helped where the patient has been beyond assistance from surgery. If Dr. Deaver finds it possible to dispose of the radium treatment of cancer by saying it is doomed, I should like to ask him in the name of humanity, what he would put in its place. What is he going to do for those suffering from cancer whom surgeons cannot help?" Speaking of the work done with radium at his own clinic, Gaylord states "No operation has been performed for cancer of the womb for three years. The records show that 34 per cent of such cases are, apparently, permanently cured, although it is impossible to state that definitely, as the disease may recur, in such cases, in three, five, ten or even twenty years. Seventeen per cent of these cases were reported favorably at the time of beginning treatment, that is, as likely to be benefited by radiation, and 17 per cent were cases in which no surgeon could offer relief by operating. Fifty per cent of those who applied for treatment at the institution are beyond cure but the radium treatment has given many of them a longer lease of life, in some cases as much as five years. Most of these hopeless cases had been given up by surgeons after operating upon them."

The foregoing quotations, coming as they do from newspaper interviews, have no scientific value but have been presented to demonstrate the attitude of some radium workers at the time of Deaver's statement.

For a more scientific discussion on the present position of radium in the study and treatment of uterine cancer, we present the work of Stone[1] whose statements are based on observations of the effects of radium in over 400 cases of uterine cancer and from the study of its effects on the tissues of other parts of the body. He states that radium in all recurrences, although less effective than in primary lesions, produces immeasurably better results than operation, provided they are not too far advanced and are not too closely related to the bladder or rectum that to cause their regression would produce fistulas or severe functional disorders. It is impossible to define the limits of growth beyond which the use of radium is undesirable, but it is essential, in order to obtain good results, to treat cases in the early stages, and, in general, good judgment demands that treatment shall cease within narrower limits of growth than is the case with primary lesions. In numerous instances, however, pain may be relieved, hemorrhage stopped, and the progress of the growth hindered by one carefully adjusted dose, when the advanced stage of the tumor precludes the idea of a considerable regression. Occasionally, also, a recurrence in less accessible parts of the pelvic

[1] Surgery, Gynecology and Obstetrics, 1921, **32**, 509.

tissue may be favorably affected by means of cross-fire radiation. For this purpose it is desirable to use a large amount of heavily filtered radium in the vaginal vault and over the abdominal wall, or, in the latter location, the x-ray may be substituted. The imbedding, also, of small tubes in deep tumor tissue without filtration and containing emanation of small radio-active value is gaining results which justify the hope that our present results may be improved. For all cases therefore, of primary uterine cancer, with few exceptions, radium should be regarded as the method of choice.

Of 34 cases, representing about 25 per cent of 139 patients who had applied to the Memorial Hospital for treatment within three months after the beginning of symptoms, a primary and complete regression was obtained in 16, or 47 per cent, and a partial but substantial regression in all of the remainder. Of another 34 cases who had applied for treatment within four to six months after the beginning of symptoms, the disease was considerably more advanced. There were 3, however, in which the growth was apparently limited to the uterine tissues, and, in all, a complete regression was obtained. In 18, or over 50 per cent, although the involvement of the extra-uterine tissues was considerable and the regression could not be regarded as complete in any, the disappearance of symptoms and restoration to normal health were evidence of the value of the treatment. An improvement followed the treatment in the majority of the others. There was no improvement in a few, and in 2 instances the patients were perhaps made worse.

In forming an estimate of the permanency of the primary results, the action of radium upon the tissues extends over such long periods, six months or more, that it is idle for the purpose of statistical study to define the condition of a case until at least one year after the treatment. Without the knowledge also gained by operation, it is difficult to define results as measured by the extent of the original lesion. There are numerous cases in Stone's series who are apparently well two or more years after the treatment has been made.

The question regarding the use of radium in the so-called borderline cases has become a subject of frequent discussion and it is in this field that Stone believes that radium has demonstrated its remarkable value. With a properly adjusted dose and form of application, radium may be expected regularly to destroy all intra-uterine tumor tissue, and it is capable of destroying extra-uterine tumor tissue to a depth fully within the limits of what is generally regarded as operable with more certainty than operation. Cases judged to be outside the limit of operability are frequently made to appear to be well within such limits after the use of radium, and the limiting of the field of operability by surgeons who are using only a comparatively small amount of the radium salt, gives ample confirmation to this opinion. The question of operating in this type of case after radium has produced an apparent regression must await the reports of final results, but the histologic changes that radium produces in the surrounding tissues shows that such a procedure is probably erroneous. If radium has caused a complete destruction of tumor tissue, operation, of course, is unnecessary. The presence of

tumor cells in the extra-uterine tissues after treatment can only be definitely known by means of the microscope, and the encasement of such cells by a fibrous framework of connective tissue will be destroyed by the knife, and the cells will thus be given the chance of renewing their original activity.

There is naturally a tendency on the part of surgeons to use radium as an adjunct to operation instead of as a substitute, either in advanced cases after removal of as much of the growth as possible, or prophylactically, in early cases immediately after operation has removed all gross evidence of the disease. In the first instance, Stone thinks its use should be discouraged since we have abundant clinical and experimental evidence that cutting through tumor tissue markedly increases the growth capacity of tumor cells, and our primary results in advanced cases show that radium can produce effects unobtainable by operation. Furthermore, we know what a favorable site for the application of radium exists in the cervical canal, and to remove the uterus takes away this advantageous position, and so greatly diminishes the chance of success with this agent. In early cancer of the cervix the primary results already obtained give undoubted evidence of its remarkable value. Lymphnode involvement, however, although it does not have the same relative importance as in many other locations, is a factor in a definite percentage of cases, and there is no way of definitely ascertaining the involvement of these nodes except by exploratory operation. We are not yet able to depend upon the x-ray or radium to prevent invasion of lymph nodes or to cause their disappearance if involved, therefore radium cannot entirely supplant the operation in all of such early lesions of the cervix. Stone states that in general, the chief error in the use of radium is overdosage, by which the nutrition of the neighboring normal tissues is so altered that reparation is postponed or entirely prevented. Failure to recognize how many weeks or months the action of radium upon the tissues persists often leads to a premature repetition of the treatment and a disastrous result that might otherwise have been successful. Lastly, a strong plea is made to avoid treatment of primary cases that are too far advanced. Unless this warning is generally and promptly heeded, much unnecessary suffering will continue to result and radium will soon be as discredited as is the operation, in the eyes of the public. There are numerous primary cases in which the general health appears to be little, if at all, affected, but in which the local lesion has advanced so far that all of the normal anatomical relations of the pelvic structures are obliterated. To treat such cases will result only in the premature production of the terminal stage of the disease.

In these days when so much is said in favor of radium and almost as much is said against its use, we are greatly interested in obtaining the opinions of level-headed men who are neither radium enthusiasts nor operative maniacs. It is therefore of interest as well as of much importance to the profession to note that Graves[1] uses radium for the treatment of cervical cancer only in inoperable cases. It should also be noted

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[1] Surgical Clinics of North America, June, 1921, p. 615.

however, that since the advent of radium, his definition of what is operable and what is inoperable in cervical cancer has undergone some modification. Formerly, he regarded as operable a case of cancer wherein it appeared possible to perform a radical operation without killing the patient or without mutilating the hollow organs of the pelvis, even though it seemed probable that a permanent cure of the disease could not be effected. This policy was pursued because such operations usually palliated the patient's symptoms and often prolonged her life to a considerable extent. Since the acquisition of radium he has come to define as operable only those cases in which a radical operation offers some chance of obtaining a permanent cure. This viewpoint has been reached because he has found that in these sub-borderline cases radium sometimes, though not always, produces palliative results equal to those of radical operation, and does not subject the patient to operative risk. He has not yet become convinced that in an operable case (or perhaps one should say a *curable* case) we are giving the patient as good a chance for ultimate cure by radium as we are by operation. Graves has only 100 milligrams of radium and although this amount has been of inestimable benefit as a palliative agent, it has not infrequently proved unreliable and treacherous and therefore is convinced that his equipment is too meager to warrant its use in a frankly operable case.

A REPORT FROM AN EMANATION LABORATORY is of interest in contradistinction to most of the reports which are based upon the use of radium itself rather than its emanations. Such a report has been presented by Duncan[1] who has at his disposal approximately one gram of radium element and a thoroughly equipped emanation laboratory. He states that his results have improved consistently with the increase in his experience and facilities. During the past three years he has continuously employed a larger dosage with heavier screening producing less tissue destruction and more effective radiation of the entire pelvis, as evidenced by the clinical changes resulting. He is convinced that large quantities of radium or radium emanation are necessary and he employs applicators containing from 200 to 500 millicuries, which are left *in situ* for from ten to twenty hours, at each application. The total dosage employing both vaginal and intra-uterine applications averages from 6000 to 10,000 millicurie hours. As a rule, the treatment is given in from two to four applications, made at intervals of forty-eight hours, thus requiring the patient to remain in the hospital on an average of less than one week. In certain cases he has found it desirable to bury within the tumor mass a number of emanation needles containing approximately 50 millicuries each and screened with 0.5 mm. of platinum. These needles are placed at a distance of approximately 3 cm. and are allowed to remain *in situ* for ten hours. In certain other cases he buries a number of bare emanation tubes of small activity which are not removed. Needles may be employed alone or in conjunction with the vaginal or intra-uterine applicators. More recently, he has employed, in addition to the local application of radium, massive doses of radium externally or

[1] Journal of the American Medical Association, 1921, **77**, 604.

deep roentgen therapy, but thus far these applications are of unproved value.

Notwithstanding a rapid absorption of carcinomatous tissue in many cases, there has been little immediate constitutional disturbance from toxemia or other causes, in fact in a majority of cases a rapid and marked improvement in the constitutional condition and blood picture is shown. The bladder and rectum are thoroughly emptied before each application of radium, and by the use of a pack are held well away from the vaginal application. There has been very little annoyance from bladder irritation, though in cases in which there is involvement of the posterior vaginal wall a more or less severe rectal tenesmus develops about ten days after treatment and continues for about two weeks. From the treatment there results more or less temporary inflammatory reaction followed by a gradual absorption of the cancer tissue. The vaginal ulceration and new growth disappear, the cervix shows local healing and more or less absorption where it has been extensively involved. The uterus reduces in size and, due to changes in the parametrium, becomes less fixed. Such improvement gradually progresses, resulting in a more or less complete recovery. Six or ten weeks must elapse before the reaction has entirely subsided and the effect of treatment is complete. Subsequent treatment may be given if indicated, but care is necessary in applying radium to a scar resulting from a previous radiation, surgery, or cauterization. Primary curettage or cauterization is not beneficial and, in certain cases, aggravates the after-treatment symptoms and sequelæ. I heartily agree with Duncan in the statement that surgery following an apparent cure from radium is not only unnecessary but frequently disastrous. The summary of results obtained by Duncan in his series of 236 cases of uterine carcinoma shows that 106 are dead, 24 improved, 10 not traced, 96, or 40.6 per cent. clinically well. In accepting these figures it should be remembered that none of the living patients has yet passed the five-year mark, in fact only 7 cases have passed the four-year mark. However, he is very enthusiastic about his work and believes that uterine cancer, when given early and appropriate treatment, is curable in a large•percentage of cases. Furthermore, appropriate radium therapy in recurrent and inoperable carcinoma surpasses, in his opinion, any known therapeutic agent and when employed by one with adequate facilities, skill and experience, is the treatment of choice in early, or so-called operable, carcinoma of the cervix. Of course, this latter opinion is still questioned by both surgeons as well as by many radium workers.

BRITISH REPORT ON RADIUM. In a paper presented by Burrows,[1] from the Manchester and District Radium Institute, Royal Infirmary, Manchester, England, only the treatment of advanced carcinoma of the cervix is discussed because, until recently, all the cases which he had treated had been beyond operation. He states that there is no necessity for the heavy metal screening which has been employed by the radiologists and a screen thicker than 1 mm. silver need never be employed

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[1] British Medical Journal, October 1, 1921, 524.

unless huge doses of radium are to be used. In the screened method in use at Manchester about seven tubes are inserted under an anesthetic. A large one of about 50 millicuries of emanation screened by 1 mm. of silver is introduced well into the cervical canal. Six other smaller tubes screened by 0.3 mm. brass are pushed into or about the cervical growth, care being taken to introduce two or three into the broad ligaments. The strength of each of these smaller tubes is about 15 millicuries. If consistently good results are to be obtained, a dose of never less than 120 millicuries for twenty-four hours must be given. In employing the unscreened method, he still uses the large central tube mentioned above, but inserts in the surrounding tissues small unscreened capillary glass tubes, each containing radium emanation of a strength of 2 to 5 or even occasionally 7 millicuries. They are inserted to the number of two to eight by means of an exploring syringe needle and stylet. No effort is made to withdraw the small tubes, but the large one is withdrawn after twenty-four hours. The vagina is always packed with gauze after the insertion of the radium in order to maintain the tubes in position. Occasionally this packing produces retention of urine, and catheterization is necessary. Douching should be performed daily after the operation—first and most important, to keep as clean as possible the reacting growth and secondly, though not now so important since the tubes have been buried and not merely placed in the vagina, to prevent the formation of vaginal adhesions.

The outlook is not good when the growth is very large and hard since with adequate treatment it tends to slough, with inadequate treatment nothing happens to the patient's advantage. Large fungating growths do not matter. Cases with very extensive infiltration of the vaginal wall rarely give a good result, even from the point of view of palliation. Burrows is yet to be convinced that the exact histology of the carcinoma is of much help in the prognosis of cases, but of course those tumors which form metastases rapidly give the worst results, and it is probably for that reason that the outlook for women under forty is bad whatever the stage of the disease, while the prognosis improves as the menopause is approached or passed. For the best results cases just beyond operability, as might be expected, are the best, but the presence of some slight mobility of the uterus, a good blood supply to the tumor, and the slow formation of secondary growths, are all factors of good omen. The more firmly the growth is adherent to the bladder and the greater the infiltration of the bladder wall and urethra, the more chance is there of a fistula resulting from the treatment; but the percentage is low (in fact, very little above that of untreated cases), and adhesion to the bladder by no means renders the case hopeless. In estimating the immediate results of radium treatment, with an eye to the future progress of a case, a very high standard must be set. The patient in a so-called "symptomatic cure" should profess to feel perfectly well and to be absolutely free from pain or discharge. Examination should show the uterus to be quite mobile, while the cervix should be small and smooth, and any scar tissue soft and supple. Vague pain in the abdomen, back or limbs, slight induration in the vault of the vagina, enlargement and hardness of the cervix, are all factors

which promise recurrence. It is interesting, however, to note that sometimes recurrence may not be manifest for several years. During the past two or three years Burrows has been able to obtain microscopic examinations of a number of cases of carcinoma of the cervix which have been treated first by radium, the uterus being removed six to twelve weeks later. It is interesting to note that in most of the cases the growth in the cervix has completely disappeared and been replaced by the characteristic dense radiation connective tissue. Occasionally, a few degenerate malignant cells are seen.

METHOD OF RETAINING RADIUM IN THE CERVIX. There is sometimes an uncertainty of accurate retention of the radium tube in the cervix and uterus by gauze packing, while if the radium is sutured in
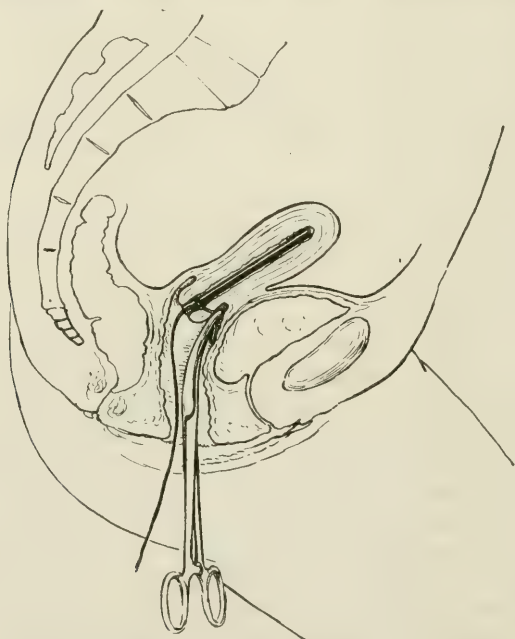
FIG. 1.—Method of retaining radium. (Furniss.)

place in the usual manner there is difficulty of removal. To overcome these factors, a method of application has been devised by Furniss[1] which consists of placing the radium tube in a 1 mm. black rubber tube, after which the tube is tightly tied with linen thread above and below the radium. After the location desired has been determined, a long linen ligature is tied around the tube at the proper point, both ends being left long. One end is threaded on a surgical needle and passed through the anterior lip of the cervix from within outward. A straight artery clamp is then applied to the suture at the point where it comes through the lip of the cervix and this ligature is cut short on the distal side. The other end of the suture hangs over the vulva. The vagina is packed

[1] Journal of the American Medical Association, 1921, **77**, 623.

with gauze to prevent pressure and to furnish proper protection from the radium. To remove the radium, the gauze packing is extracted, the clamp released and the uncut end of the ligature pulled.

HISTOLOGIC STUDY OF RADIUM EFFECT ON CANCER. The exact effect of radium treatment on the carcinoma cells, as determined by histologic studies upon radiated tissues, has been determined by Norris and Rothschild[1] who divide the histologic pictures into five stages. The first stage is that of acute inflammatory reaction and embraces the first week after radiation. During this stage there is a congestion of the bloodvessels, exudation of lymphocytes and polymorphonuclear leukocytes, and a slight edema of the stroma. A slight swelling of the cancer cells is noted, also slight enlargement of the endothelium of the bloodvessels. The second period embraces the second week and is the stage of early nuclear and cytoplasmic changes. This stage shows a gradual swelling of the cancer cells, an enlargement of the nuclei and relative increase of the cytoplasm. Mitosis in many instances ceases and the nuclear substance appears as granules, while the cytoplasm at times shows vacuolization. At the beginning of the third week, the stage of intercellular changes, young fibroblasts are found scattered throughout the radiated area. They infiltrate the malignant cells, dividing them into strands and in many instances completely surrounding groups of cancer cells and isolating them. The lymphocytic infiltration is increased in this stage, although lymphocytes and leukocytes have been present during the first two weeks. The bloodvessels show edema of all the coats and especially of the intima, with almost complete obliteration of the lumen. At times, leukocytes are present in the vessel wall. The stage of destruction starts with the fourth week after the application of the radium and continues to the ninth week. The nuclei of the malignant cells may be broken up and in many instances found as masses of chromatin, while, on the other hand, they may shrink and appear as an egg in a nest. The cytoplasm undergoes cytolysis. The group of cancer cells which have been isolated by the fibroblasts and connective tissue show a numerical reduction. The fibrous overgrowth at the end of this period is conspicuous. In its meshes the young bloodvessels at times show constriction of the lumen while the malignant cells throughout the entire field are considerably reduced numerically and in size. In the final period or stage of healing, the cancer cells appear as compressed bands in the fibrous stroma, only the small contracted nuclei remaining. At a later period, no remains of the malignant cells are noted. Ultimately, the surface epithelium shows regeneration. The features of these changes are the changes of the malignant cells with their destruction and ultimate absorption and the replacement by fibrous tissue. While the histologic pictures have been divided into five stages, it must be acknowledged that the stages blend, and one may find many instances of early cellular changes with cells in the stage of destruction.

[1] American Journal of Roentgenology, 1921, **8**, 604.

Personal Views on Radium[1]   From time to time during the past five years Keene and I have recorded in the current medical periodicals our results from the treatment of cancer of the pelvic organs, particularly of the uterus, with radium, and in these articles we have dwelt especially on the palliative effect of radiation rather than to hazard a discussion as to the possibilities of ultimate cures, notwithstanding the justifiable hopes as to this outcome.   We have maintained this position because of the skepticism which the world holds as to the settlement of this age-long quest for a dependable remedy for cancer.   Today we may assert with positive assurance that even in the inoperable case of carcinoma of the cervix a surprising number, as reckoned by the quinquennial test, have survived and are quite free from any demonstrable or symptomatic evidence of cancer.   Those patients that are alive and well were registered in our clinic during the first years of our work with radium, while methods were largely in the proving ground, for we then knew little of the dangers and range of action of this occult force.   In view of the fact that these cruder attempts have yielded a definite percentage of cures, we feel greatly encouraged; for with improvements in application and with a consequent lessening of bad sequelæ, a decidedly better outcome may be forecast as these later series come up for review.   In order that there should be no conflict in our report between the more recent and the older cases, we have included in this present report only those treated before August, 1920, a total of 313 cases, 112 of whom are living and 201 dead.   All of our patients have been subjected to 100 mg. of radium for twenty-four hours at the first application, and this dosage may therefore be considered as the standard to which we have adhered with only an occasional exception.   We have purposely held to this standard because the primary results in our first 100 cases appeared to be so satisfactory in promoting relief of the chief symptoms of cancer that it seemed injudicious to change it radically.   As several workers in irradiation have used different dosages, both as to quantity, duration of application, and repetitions of treatments, and since we are all in accord as to the primary palliative results, it seemed best for us to pursue this course in our clinic so that when we all assemble our reports for critical review, we may judge as to the best way of synchronizing methods and arriving at a uniform plan of activity among those clinics in which the larger and smaller quantities are available.   Our plan through at least 150 cases was to apply 100 mg. contained in a glass capsule and this in a platinum tube, and this in turn enclosed in black rubber tubing, for twenty-four hours in immediate contact with the cervix, the healthy adjacent tissues being shielded from undue injury with lead protectors.   After a six weeks' interval, this procedure was repeated.   As to the results, we found that several patients sustained burns of sufficient intensity to cause much irritability of the bladder, or an acute proctitis occasionally causing pain varying from a mild and fleeting character to that of severe and persistent intensity.   While this was by no means a uniform sequel, it occurred with sufficient fre-

[1] Journal of the American Medical Association, 1921, **77**, 613.

quency to be a decided disadvantage and a trying and discouraging ordeal for the patient. Added to this immediate effect came the later and much graver complication, a rectal or vesical fistula in some instances which are always obstinate and even intractable to healing either by operation or through the expectant policy.

Among our living patients, 112 cases, 13 have had fistulas; of the 201 dead, 21 were noted sooner or later before death. As to the living patients, we attribute practically all to the effects of irradiation, but this acknowledgement does not constitute a condemnation but a warning, to which we shall refer later. Among the 201 dead patients, we consider only 21 fistulas, approximately 10 per cent, as a definite triumph for irradiation, for among those who ultimately succumbed there were 10 in whom the local healing was maintained to the end, the patients dying of metastases. The assertion that had the same number of inoperable cases reached the end without irradiation, fistulas in a considerable larger number should have been a natural incidence of the cancerous invasion of the bladder or rectum, does not appear as questionable but rather as the statement of a fact. Our position, therefore, is that while radium actually does produce fistulas in a small percentage of patients, on the whole it actually defends a much larger ratio against this complication. To remain contented with this adjustment of equations is, however, not our desire, and to obviate this very disabling accident, we have completely discarded all metal protectors in vaginal applications, and instead use gauze packing. For this suggestion we are indebted to Burnam. By far the larger number of fistulas date back to the period of lead protectors, but with our present plan we have much less apprehension as to this possible complication.

We have discovered that in a considerable proportion of cases the lethal blow to cancer of the cervix is given by the first impact of the radium, and the question has arisen: Do repeated applications make assurance doubly sure, or may they not occasionally jeopardize a successful issue? We are not fully prepared to answer this query, but we are convinced that the routine repetition of treatments is injudicious without taking into account the results of the first treatment. For instance, in one class of patients reporting six weeks after the initial application, we find remarkable local healing in process of completion; in another the ulceration appears to be *in statu quo*, while in a third no apparent beneficial effect is evident; on the contrary, a definite failure to hold in check the ulceration is obvious. In the occasional case we believe that there is an actual acceleration of the growth, especially in advanced extensive cases and we are inclined to limit its employment to those cases in which there is visible or palpable localization of the gross changes. When there is a deep crater occupying the site of the lower uterine segment and extending out to the pelvic walls and backward and forward to the rectal and vesical walls, with grave cachexia and other evidence of metastasis, we may by this treatment actually render more wretched the few remaining weeks of existence of these patients. Also, when there are fixed pelvic masses extending out to the iliac walls, very seldom can anything be accomplished, for the destructive changes are

too far removed from the focus of irradiation for even palliative measures. As we are not employing the emanations we cannot speak as to results in these cases when the glass tubes are embedded in the malignant mass.

In those cases in which a progressive favorable action is noted six weeks after the initial treatment, not infrequently the patient is advised to return again in six weeks, and if then we find a white, hyaline cicatrix fully covering the site of the ulcer, we further delay action and may not see the patient again for six months. In the second class of cases in which no progress is noted, we usually make one more application and await the turn of events at the end of another six weeks' interval. At that time should no progress be noted, further irradiation is abandoned, for we class such cases as hopeless. Within our knowledge no favorable turn has been noted from a third application if the first two have been unsuccessful and to repeat the treatments only adds to the patients distress. Here, as is observed with any operation in the hopeless case, the remedy may be severely condemned, thus generating a prejudice among the relatives or friends of the patient which may subsequently block its use in some other favorable case.

Another modification in our method of application deserves special mention. In the first three years of our experience, we were content to make the application without the aid of an anesthetic. A bit of tissue was snipped off or gently curetted away for confirmative diagnostic purposes, and the radium was then applied usually with the patient in the Sims, or knee-breast, position. Under these conditions it was frequently difficult to adjust the radium tube accurately to the affected area. In applying the metallic vaginal shields, or in later cases, the gauze pack, the tube might shift and thus cause trouble. To obviate these dangers and to be certain of a complete orientation at the first sitting, nitrous oxide anesthesia is administered. If there is a large cauliflower mass, it is excised by the cautery. By this procedure radium may be brought one or more inches nearer the crucial area, thus securing full contact and avoiding the rapidly lessening effect of the intensive irradiation as the distance is increased. Further, when possible, we always insert a 50 mg. tube within the cervix and a cross contact tube of equal quantity in the cervical crater or vaginal vault. Not infrequently a superficial cone-like incision is made with the cautery, avoiding a deep penetration into healthy tissues, and the radium tubes are enclosed within this cup with fine catgut sutures. As to the use of radium needles, our experience is as yet too limited to warrant any positive assertion as to their value in cervical cases, but we anticipate a betterment of statistics from this source of deeper irradiation. Since cancer extends by the broad and utero-sacral ligaments, we not infrequently insert four needles of about 13 mg. each into these structures. Obviously, the danger of injuring the rectum or perforating Douglas' cul-de-sac attends the penetration of the utero-sacral ligaments, while the ureters or uterine vessels are jeopardized in the broad ligaments. Through the guidance of the needle with one finger in the rectum, and directing the needle slightly posterior and outward in the broad ligaments, these dangers may largely be obviated.

In cancer of the fundus, we always incline, even in advanced cases, to operation. In this connection, we simply reiterate what has been said in previous articles: "In cancer of the cervix, when in doubt always irradiate, in cancer of the fundus, when in doubt operate." However, in cancer of the fundus, when there are grave contraindications to surgical intervention, we turn to radium with great hope when the case is within reasonable limits. In our list of 313 cases there have been only 23 cases of cancer of the fundus. Of these, 12 patients survived from three to six years without objective symptoms or demonstrable lesions. The remainder are below a three year limitation but are in excellent health. In 11 cases which were far advanced when treatment was given, the patients are dead, but there were none of these within the potentialities of the most daring surgeon. We have found no evidence whatever to incline us towards surgical intervention after successful irradiation, but quite positively in the contrary direction.

Finally, what is our attitude concerning immediate ante-operative irradiation? From dire experience we have definitely discarded this plan, and while this decision is based on a very limited experience, it was nevertheless an alarming one. The bad results occurred in 2 cases of high amputation of the cervix a day or two subsequent to a twenty-four hour irradiation. For a few days, a splendid convalescence followed; then an ugly infection, with widespread disintegration, developed in the operative area. One patient died of a slow but progressive pyemia, the other passed through a stormy convalescence but finally recovered. To devitalize tissues invaded with septic bacteria, which are not destroyed before surgical intervention, makes indeed a bad outlook for the surgeon. Possibly a very evanescent irradiation of from four to six hours in order to blight only the superficial areas and not the deep tissues might be effective in reducing implantation possibilities. Beyond this, however, we enter a zone of deepening shadow. In the event of a hysterectomy being performed, we prefer to irradiate from fourteen to twenty-one days later, after the surgical cicatrix in the vagina is fixed, and then under careful protection and only for twelve hours. The percentage of patients suffering from inoperable carcinoma of the cervix and yet living without evidence of cancer from three to four years on to six and seven years is 24 per cent. Without doubt, no other method of treatment attended with so little danger can show such excellent results. In all our series of cases, now more than 400, only 2 deaths occurred shortly after irradiation alone.

A few years ago I reviewed the final results in 59 cases of radical operation for cancer of the cervix, and the yield of quinquennial cures was about 33 per cent. In comparing the vast outlay of surgical effort put forth in the latter class of cases with the great danger attending the radical operation, as to both mortality and disabling results, we feel convinced that the time has about, if not quite, arrived when we shall cease to speak of any operable cases of cancer of the cervix but shall submit them all to irradiation. Certainly our results have led us very convincingly in this direction. As the palliative results have been so excellent and, as our statistics now appear, the actual cures have been

so relatively large in the hopeless cases, it would appear illogical to submit the early operable cases to the great dangers of surgical intervention and reserve only the inoperable case for irradiation. While we still discuss operability, we are indeed turning to this method of procedure in such a small minority of cases in our clinic as to carry our statistics in this line almost to the vanishing point. In two other classes of cases we have employed irradiation with great reluctance; and yet, as our statistics show, this pessimism is unjustifiable. From the anatomic standpoint, the hazards of fistulas are much greater when radium is employed in cases of recurrence in the vaginal vault after hysterectomy. Of this class there have been 21 cases, in 7 of which the patients are living, 5 being alive over two years. Of these, 1 has passed the three to four year period. Of the 7 living, 2 have fistulas. Among the 14 fatal cases, there were 3 fistulas. From these observations our apprehension as to fistulas is confirmed, for this class of case will undoubtedly be followed by a larger percentage of fistulas, another very telling argument against a hysterectomy in the borderline case if irradiation is subsequently to be resorted to.

This brings up the question, Should the surgeon resort to an operation in the questionable case, and then depend on irradiation to aid him? To act in the affirmative, we believe, is not only an unwise, but a positively dangerous, course. While an irradiation subsequent to a hysterectomy may save the day, it may leave in its train a distressing and possibly hopeless fistula. We cannot too urgently advise against this course. When the uterus remains as a broad wedge of tissue keeping the bladder and rectum well apart and the dome-like vault of the vagina preserved, with the carcinoma held centrally between the broad ligament, the opportunity for successful work by the radiologist is greatly enhanced. When a hysterectomy is performed, these elastic tissues may retract to the iliac walls and thus remove the cancer outside the zone of safe irradiation. A second class of cases in which cancer of a cervical stump has occurred, are those due either to oversight at the first operation or possibly to a subsequent invasion of the stump. Four such cases appear in our series, and all the patients are alive, 2 one and one-half to two years, and 2 three to four years after treatment. Is it likely that an excision of such an invaded stump could give as good, or better, results?

DANGERS OF WORKING WITH RADIUM. Now that the number of physicians who handle radium is rapidly on the increase, it may be questioned whether all of them realize the dangers to which they are subjecting themselves by constantly handling such a powerful element, and, if so, are they aware of the measures which have been recommended to protect the worker. Thus, the London correspondent of the *Journal of the American Medical Association* (1921, lxxvi, 1412) states: "Recently I reported the deaths of three workers at the Radium Institute which were attributed to aplastic anemia due to their occupation. The first death occurred in 1916 in a worker who was seen by several specialists and whose death was ascribed by them to pernicious anemia. The second death occurred in 1920 in a nurse, and was due to infective

endocarditis, but it is admitted that the radium had unquestionably affected her, though it was not from this alone that she died. The third death occurred in 1921 and was due to acute pneumonia. Each death is claimed to have been due to a definite disease apart from the effects of the radium, but the institute committee considered it highly probable that the work of these persons weakened the powers of resistance to the diseases from which they suffered. J. C. Mottram was appointed to make a special investigation of the effects of radium on the staff of the institute. For a year he made examinations of the blood of every worker, from the superintendent down to the hall porters. He found definite changes in the red and white blood corpuscles due to exposure to radium. He showed that radium workers are subject to widely different amounts of irradiation varying as they work near to, or distant from, radium and according to the period of exposure. The polymorphonuclear leukocytic and the lymphocytic blood count of radium workers was found decidedly lower than that of normal persons. The leukopenia of radium workers is manifest after a few weeks exposure." In several of the radium clinics in this country, disturbances of menstruation among the nurses were noted during the early stages of radium therapy, but this has largely been eliminated by means of transfering the nurses to other duties after they have been in close contact with radium for a month or two and after a reasonable time they are permitted to return to their work with radium patients.

In England, a committee[1] was appointed to consider radium protection and they recommended that in order to avoid injuries to the fingers, the radium, whether in the form of applicators of radium salt or of emanation tubes, should always be manipulated with forceps or similar instruments, and it should be carried from place to place in long-handled boxes lined on all sides with 1 cm. of lead. In order to avoid the penetrating rays of radium, all manipulations should be carried out as rapidly as possible, and the operator should not remain in the vicinity of radium longer than is necessary. The radium, when not in use, should be stored in an enclosure, the wall thickness of which should be equivalent to not less than 8 cm. of lead. In the handling of emanation, all manipulations should, as far as possible, be carried out during its relatively inactive state. In manipulations where emanation is likely to come into direct contact with the fingers thin rubber gloves should be worn. The escape of emanation should be very carefully guarded against, and the room in which it is prepared should be provided with an exhaust electric fan.

Combination of X-ray and Radium Treatment. Various controversies have arisen from time to time concerning the advisability of combining surgical with radiologic procedures in the treatment of uterine cancer. Also there have been discussions concerning the choice of radiation—some assert that radium rays are more effectual in killing off the disease than roentgen rays, while others state that a combination of both radium and roentgen rays assures better results. Schmitz[2]

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[1] British Medical Journal, June 25, 1921, p. 936.
[2] Journal of the American Medical Association, 1921, **77**, 608.

is a staunch supporter of this latter view. He reminds us that the object of the treatment of cancer of the uterus is the eradication or degeneration of all cancer cells without permanent injury of the neighboring healthy organs, such as the bladder, the rectum and the small bowels. The uterus is contained within the true bony pelvis and its axis corresponds, as a rule, to the axis of the true bony pelvis. The posterior bladder mucosa and the anterior rectal mucosa are from 2 to 3 cm. distant from the cervical canal. If radium is inserted into the cervical canal, the time duration of the application depends entirely on the intensity of radiation striking the bladder or rectal mucosa. For instance, 50 mg. of radium element filtered through 1.5 mm. of brass and 3 mm. of para rubber, inserted into the cervical canal, will cause an erythema of the vesical mucosa and of the rectal mucosa within thirty hours. Since the lethal amount of radiation that the rectal mucosa will bear without any permanent injury is 130, if 100 means the intensity of the dose sufficient to produce an erythema skin dose, we cannot extend the application of 50 mg. radium element beyond thirty consecutive hours, if we wish to avoid ulcers and strictures of the rectum and the like. However, in limiting the action of the radium rays, the cancer elements lying near the bony pelvic periphery are not only not degenerated but stimulated to increased activity and proliferation by the so-called "stimulating dose" of rays. After many years of careful study on this subject, Schmitz has come to the conclusion that this problem may be solved by using a combination of radium and roentgen rays. He possesses an instrument which enables him to measure the intensity of radiation emitted from a Coolidge roentgen-ray tube, so that he can measure a quantity of irradiation, which applied through only two ports of entry under like conditions sends an intensity of about 75 per cent of the skin surface intensity to the region of the cervix if the antero-posterior diameter of the pelvis is not more than 16 cm. Therefore, it is only necessary to supply the missing 25 per cent with the use of radium radiation in order to obtain an intensity of 100 all through the pelvis, it being conceded that 100 represents the intensity of radiation necessary to produce an erythema skin dose, and it being further conceded that this intensity amply suffices to degenerate cancer cells. Fifty milligrams of radium element will accomplish this very nicely with a thirty hours' application, states Schmitz, although patients with an antero-posterior diameter of more than 16 cm. may require a longer application.

Surgical Treatment of Cervical Cancer. So far as Graves[1] is aware, he has never cured a single case of cancer of the cervix with radium. He is broadminded enough, however, to state that such a statement is merely the result of individual experience and is not equivalent to saying that inoperable cancer of the cervix cannot be cured by radium, for there is evidence to the contrary. In view of the greater successes attained in other clinics than his, he believes it possible that some of his radium cases now in the so-called "clinically cured" stage may ultimately prove

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[1] Surgery, Gynecology and Obstetrics, 1921, **32**, 504.

to have been permanently cured. At the present time however, in view of the uncertain and sometimes treacherous behavior of radium in his experience, he does not feel justified in substituting it for radical surgery in cases favorable for operation. Since his first radical operation in 1909, 189 cases of cervical cancer have been seen, of which 119 have been subjected to radical operation by the abdominal route. The operability percentage, allowing for cases that refused operation, is 64 per cent. In this series of 119 operations there have been 6 deaths resulting from the operation, or an immediate mortality of 5 per cent. The five year curability percentage is 27.6 to 34.2 per cent according to the method of computation, while the absolute curability is 16.8 to 18.5 per cent. In 101 of the 119 operations, the Wertheim technic was carried out more or less completely. In the other 18 operations no attempt was made to follow the special Wertheim technic, the steps of the operation being practically those of the ordinary complete hysterectomy, with the amputation of the vagina made as low as possible. Of post-operative sequelæ due to injury of the hollow organs of the pelvis, there have been 2, 1 vesico-vaginal and 1 recto-vaginal fistula. The percentage of post-operative fistulæ is therefore 1.7 per cent. Graves does not claim these figures are spectacular but they are offered because he thinks that they represent a fair index of the present status of the surgical treatment of operable cancer of the cervix. The radical operation has been criticized as being too difficult for practical use. Graves agrees that it is unquestionably difficult and should not be attempted until one has acquired a considerable amount of operative skill. The days of reckless resection of ureters and bladders, and vast bloody dissections of the pelvis are long gone by. Such operations are only palliative except in rare instances. Surgeons now are adopting a saner conservatism both in the choice of cases and in the technic of the operation, hence the lower mortality, excellent convalescences, and freedom from disabling post-operative sequelæ.

Deaver[1], as would be expected, states that in the presence of undoubted cancer, complete hysterectomy is probably as sure a means of curing the disease as we have, provided, of course, that the growth is not so far advanced as to threaten adjacent tissues. He states that he bases his remarks on a series of 500 hysterectomies that he has performed during the past five years. On close analysis of his 500 cases, it is readily seen that *only 27* of these operations were performed for cancer of the uterus, which merely again emphasizes the fact that some statistics are not of as much value as they would, at first glance, seem to indicate.

In the opinion of Weiss[2], cancer of the cervix is still to be classed as an operative condition when discovered early and the patient is a good risk, When a doubtful borderline condition is presented, treatment by radium is advisable he believes, and the question of subsequent operation should be determined by the reaction obtained; but if operation is contraindicated by age, general condition, heart, kidney or bloodvessel,

[1] American Journal of Medical Sciences, 1921, **161**, 661.
[2] American Journal of Obstetrics and Gynecology, 1921, **1**, 661.

radium alone should be used. A careful comparison between the cautery and radium type of treatment shows that both have advantages and disadvantages, and that, in carefully selected borderline cases, far better results are obtained by him by a judicious combination of cautery amputation followed by moderate doses of radium. Weiss' results in a small series of borderline cases, while generally satisfactory, are far from conclusive. Similarly, the wide range of radium dosage in treating cervical cancer, varying from 1500 mg. hours in some clinics to 8000 mg. hours in others shows that no definite conclusions have been reached, and while favorable reports have been received from both extremes, the use of radium is still somewhat empirical, in his opinion.

Incidence of Cancer in Retained Cervical Stump. Paraphrasing Hamlet's famous soliloquy to the realm of gynecology we might say, with respect to the type of hysterectomy that should be performed in removing uterine fibroids, "complete or incomplete" and indeed it is quite a question, since both sides have their noted advocates. Polak[1] reminds us that squamous cell cancer primarily starts from the squamous epithelium covering the mucous membrane of the vaginal portion of the cervix, while adenocarcinoma either develops from cylindric epithelium covering the mucosa of the canal, or from that lining the glands of the cervix. These facts have a clinical significance when supracervical hysterectomy is employed as the routine procedure for the treatment of fibroid tumors of the uterus, for notwithstanding the habit of some operators to cauterize or cone out the cervical canal after supracervical amputation, the areas in the cervix from which cancer usually originates are not destroyed. Comparing his own mortality in 100 supracervical amputations, against 100 total extirpations, the figures are 1.5 for the supracervical procedure against 2 per cent for the total removal. In reviewing the reported cases and those reported in personal communications, Polak finds that the occurrence of cervical cancer in the retained cervical stump is by no means uncommon, and, as might be expected, it occurs at the age at which cancer usually attacks. As a result of his investigation into this subject, he concludes that cancer occurring in the retained cervix after supracervical operations for fibroids is a clinical and pathologic entity and that it may be stated that cancer of the cervix occurs in approximately 2 per cent of cases of fibroid tumors of the uterus. The great majority of these cases occur at the cancer age, namely between forty and fifty, and in cervices that have been traumatized by childbirth or have been the seat of chronic cervical inflammation. The great majority occur in the portio or just within the external os and are squamous cell cancer, hence their point of origin is not removed by coning out the cervix. The interval of occurrence, excluding those cases in which the cancer probably coexisted at the time of operation, has varied from five to twenty-one years after the original operation. Consequently one cannot state positively that a given case of fibroid where the tumor is removed by the supracervical method, has not or will not have cancer changes in the cervix. Polak believes, therefore,

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[1] New York State Journal of Medicine, 1921, **21**, 45.

that the routine employment of supracervical hysterectomy in those fibroids which need operation should be abandoned, and that partial removal of the uterus should only be employed when the cervix is free from injury or disease in the nulliparous woman.

NON-MALIGNANT CONDITIONS OF THE UTERUS.

Radiotherapy. The present status of radiotherapy of *non-malignant uterine bleeding* has been fairly well summarized by Graves[1] who reminds us that before the advent of radium, uterine bleeding in adolescence and young womanhood presented a baffling problem. The etiology of this condition has never been solved. One may speak of ovarian hyperfunction as a cause, but the term is based on the vaguest kind of knowledge and even if it is correctly used it is of no assistance in the problem of treatment. The various remedies for this condition, such as animal serums, gland extracts like pituitrin, the various styptics, iron, arsenic, etc., are all of very equivocal value and repeated curettings are equally useless. The bleeding not infrequently continues for years and may reduce the patient to an extreme state of anemia, in some cases the surgeon being obliged to resort to hysterectomy or castration. In the earlier days of radium as a therapeutic agent, it was applied only for the menorrhagias of women comparatively near the menopause. Operators were fearful of using it in young women on account of the danger of bringing about an artificial menopause. It was soon discovered that when radium was given in moderate dosage excessive menstruation may be diminished and regulated with a fair degree of certainty. Therefore at the present time it is employed without hesitation for urgent cases, even in pubescent girls. In making the decision as to the treatment of a very young patient, the question of the danger of causing a complete cessation of the menses has been a most important one, but Graves is convinced by experience that a dosage of 25 milligrams for from four to six hours may be given with entire safety and he believes that it is quite probable that the ovaries of the young are able to withstand a greater exposure to radiation without losing their function than are the ovaries of older women.

In regard to the manner in which radium produces its effect, he believes with many others that the rays exert an influence on the endometrium as well as on the ovaries. The exact effect on the endometrium has not been determined since microscopic examination upon the uteri removed after unsuccessful treatment with radium reveal no very definite changes. One would expect a sclerosis of the stroma which might bring about a temporary or permanent obliteration of the endometrial capillaries. Radium given in sufficiently large doses is capable of destroying the Graafian follicles as has been shown by the examination of ovaries removed after the radium treatment. The extent of the destruction of the follicles depends on the size and length of time of dosage and also on the age of the patient. The primordial follicles

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[1] Surgical Clinics of North America, June, 1921, p. 620.

are formed near the center of the ovary and as they develop they migrate toward the surface, finally culminating in a ripe corpus luteum or an atretic follicle   A large dose of radium is sufficient to destroy all of the follicles in the ovary both young and old, but it may be imagined that a moderate dose may kill only the older and riper follicles that are near the surface while the younger and less developed bodies escape its influence. In this way may be explained those cases in which the menstrual function is suspended for several months, only to be resumed in a natural manner. In other words, menstruation ceases during the time required by the younger follicles to mature.   The fact that the menstruation is in most cases restored without the abnormal bleeding which before characterized it may be explained by some minute, but permanent, change in the endometrium.

Until within the most recent past, the treatment of *fibroids* has been almost exclusively surgical, and the results achieved have been eminently satisfactory.   Every decade has seen a material reduction in the mortality after operations for fibroids, but even in the hands of excellent surgeons there is yet an average mortality of from 3 to 5 per cent and if we consider all the cases operated upon, we would probably find a considerably higher percentage. Contrast with this the fact that radiotherapy has a mortality of zero.   To be sure, the word "cure" means something different in the two methods, according to Gellhorn[1] who calls attention to the fact that we obtain a cure after operation if we remove the fibroid and the patient survives and is well thereafter.   In radiotherapy, on the other hand, we aim at only a *clinical* cure, that is to say, the object to be accomplished is attained, if the menorrhagia caused by the fibroid either ceases altogether or only a scanty or infrequent flow ensues.   Furthermore, a reduction in the size of the tumor is a part, though not an essential one, of the clinical cure after radiotherapy.

With these definitions in mind, we must approach the statistics thus far published.   Many thousands of cases of fibroids have already been treated with radium or *x*-rays and the results obtained show, on the whole, a marked similarity.   In order not to quote too many figures Gellhorn mentions the collective statistics of 2982 cases of fibroids treated with *x*-rays, in which there were 95.6 per cent cures and 4.4 per cent failures.   In 944 fibroids treated with radium there were 94.4 per cent cures and 5.6 per cent failures.   These statistics taken into consideration the results obtained in various parts of the world and they include the cases in which the technic had to be first acquired as well as those in which the technic had attained its present state of refinement. If only the latter kind were tabulated, Gauss and Friedrich found that in 425 fibroids *x*-ray treatment yielded 98.4 per cent cures and had only 1.6 per cent failures and exactly the same result was obtained in 372 fibroids treated with radium.   It is important to remember that this type of treatment must not be given to fibroids which extend above the umbilicus.   Large, pedunculated, subserous or submucous fibroids are

[1] Journal of Missouri State Medical Association, 1921, **18**, 220.

likewise unsuited. In these three categories radiotherapy may produce a necrosis of the tumors. Cervical fibroids are refractory to radioactive treatment. Rapidly, growing fibroid suggestive of sarcomatous degeneration, suppurating or gangrenous fibroids, or those in which any other form of degeneration has taken place are to be operated on, likewise those associated with carcinoma of the uterus. Fibroids pressing heavily upon the bladder or rectum had better be removed surgically. It is important, therefore, to carefully select the cases which are to be radiated since the man who administers radiotherapy indiscriminately, disregards the best interests of his patients as much as the man who adheres exclusively to surgery.

As a result of a follow-up investigation in a series of 58 cases of benign pathologic conditions of the uterus which were subjected to radium therapy, Payne[1] is convinced that radium is the treatment of choice in all cases of *small myomata* whose only symptom is hemorrhage and in all types of myopathic hemorrhage and in all types of uncomplicated leucorrhea. In his work he noticed that immediate cessation of the periods occurred in about 40 per cent of the cases; there were two or more periods in about 23 per cent of the cases and there was a return to normal with regular periods in about 15 per cent of the cases. In about 5 per cent of those cases in which immediate cessation of the bleeding occurred, there has been a return after a period of about one year which has been readily controlled with a second dose of radium. There is usually a profuse leucorrheal discharge following large doses of radium in about 19 per cent of the cases and a slight leucorrheal discharge continuing for about six to eight weeks in about 26 per cent of the cases. Pain coming on after the third day and lasting about a week occurred in about 25 per cent of the cases. In women above forty years of age or in those cases where larger doses have been given, about 50 per cent of them showed symptoms of the menopause following their treatment.

One of the most comprehensive reports of radiotherapy of non-malignant uterine conditions which has appeared during the past year is that submitted by Jones[2] which is based on several hundred cases radiated by Watkins, Curtis and himself. There were 120 cases of fibroids in the series and because the dividing line between these cases and those considered in the hemorrhage group is not always definite—the principal symptom in each being bleeding—only patients with definitely palpable uterine fibroids were included. He states that the successful treatment of fibroids with radium hinges on the careful selection of cases. Tumors larger than the size of a three months' pregnancy are better treated by surgical removal, either supravaginal hysterectomy or myomectomy; pedunculated fibroids as well as the smaller intramural ones which are complicated by adhesions or tubal disease, are removed surgically. The age of the patient must be kept constantly in mind in deciding for or against radium treatment, as it is necessary to bring on a permanent menopause if the symptoms are to be relieved and the fibroid controlled. Realizing this fact, only patients approximately forty years of age or

[1] Virginia Medical Monthly, 1921, **47**, 525.
[2] Surgery, Gynecology and Obstetrics, 1921, **33**, 409.

more have been treated with radium by these men as they believe that surgical removal renders better service to younger patients. They find that the postoperative course is about the same as that following any curettage except that the serous discharge is usually more profuse and persists for a longer period of time. The menstrual reaction after radium varies with individuals; some do not have any periods after treatment, while others have as many as three, usually decreasing in amount. The menopause precipitated is more acute than the normal one, but seems to yield rather readily to corpus luteum or ovarian residue. Very little change in the size of the uterus can be detected before the twelfth week, after which the contraction is rather rapid. It has been necessary to repeat the radium in 7 cases in this series. Of all the fibroids treated, 69.1 per cent have been entirely relieved of symptoms for over two years. Not enough time has elapsed since the treatment of 22.1 per cent of cases to classify them other than as improved.

In no other division of radium treatment is it so necessary take into consideration so many different factors in the regulation of the dosage as in the patients still in the active child-bearing age who are suffering from so-called idiopathic hemorrhage. There were 129 such cases in this series. Radium insertion should not be resorted to in these cases until organotherapy has been given a thorough trial. The dose that in one patient produces only a reduction of the periods to normal or a temporary amenorrhea, might possibly produce a permanent menopause in a patient with less radium tolerance, while on the other hand, a very small dose may only increase the flow, meaning in the one an insufficient radiation but in the other a prodrome of the menopause. Careful observation of the blood pressure and tabulation of the nervous symptoms are valuable aids in the diagnosis of the approaching menopause. From 750 to 1000 millicurie hours is the maximum dose for the average individual. However, it is considered better to give initial doses of about 250 millicurie hours and repeat after three or more months if necessary, rather than to produce a period of amenorrhea. In the bleeding of the menopause, radium is practically specific, one treatment of 1000 millicurie hours with 2 mm. gold screen, equivalent to 600 millicuries hours with single screen, being sufficient in most cases to bring on the permanent menopause. The symptoms are here also somewhat more acute but fairly easily controlled. The first menstrual period is often profuse, the second less, and rarely does the third amount to more than a spotting. Eighty-one per cent of the cases in this series have remained relieved of symptoms over two years, while 16 per cent have been relieved but not sufficient time has elapsed to be sure of cure.

Jones mentions the work of Curtis, who has been trying *radium in the treatment of chronic leucorrhea.* Of the 60 cases which he has treated, 36 are now cured, 11 are improving, 10 not having been treated sufficiently and not enough time elapsing are classified as doubtful, while 3 cases have not only been cured of their discharge but have since become pregnant. Four patients have at present symptoms of an approaching menopause. The results as a whole have been highly

satisfactory and undoubtedly continued study of cases and compilation of results will prove that in chronic leucorrhea radium is one of the most valuable therapeutic agents. The technic consists of slitting open and fulgurating Skene's ducts and destroying periurethral and Bartholin's glands when infected. Following this, two 25 mg. radium capsules, $\frac{1}{2}$ mm. gold screen, and covered with rubber tissue are sutured in the cervix for about six hours.

Roentgen Therapy. The *treatment of uterine bleeding* due to *chronic metritis* or *myomata* by means of the roentgen ray, either by itself or in combination with radium, has again assumed an important place in our therapeutic armamentarium as evidenced by the numerous literary contributions on this subject during the past year. A most rational presentation of this subject has emanated from Eden and Provis[1] based upon 46 cases of fibroids and 30 cases of chronic metritis treated by the x-ray alone. They have rarely treated patients under thirty-eight years of age by this means, because the effect of the rays is exerted primarily upon the ovaries, resulting in more or less complete destruction of the active ovarian tissues. Fibroid tumors which exceed the level of the umbilicus in height have generally been rejected. Nearly all fibroids shrink in size after exposure to the x-rays, but the shrinkage of large tumors may not be sufficient to relieve mechanical symptoms. They have found that while in such cases it may be practicable to induce complete amenorrhea, the tumor may cause so much discomfort from its bulk that only partial relief from symptoms is obtained. The character of the hemorrhage is important when it raises the suspicion of malignancy. If the type of menorrhagia is not maintained, and irregular or interval bleeding is present, the uterus should be first explored to exclude carcinoma of the body. The first or even the second treatment may be followed by increased bleeding, so that in the case of a patient profoundly exsanguinated from repeated hemorrhages they believe that it is safer to perform hysterectomy. Only simple and uncomplicated cases are suitable for the x-rays and a careful examination of the cervix should be made in every case, to exclude appearances suggestive of a malignant growth. The presence of pain is a symptom which requires careful investigation; tenderness or rapid increase in size of a fibroid suggest degenerative changes; limitation of mobility or the presence of a tender swelling on either side of the uterus suggests inflammatory disease of the appendages and any of these conditions render the case unsuitable. It is evident from the foregoing teaching that they have not used x-rays as a general substitute for hysterectomy, but have, on the contrary, limited its application to carefully selected conditions and they state that the cases treated constituted only a small proportion of the fibroid tumors which have come under their notice.

The technic adopted in the majority of cases was a modification of that used in Kroenig's clinic at Freiburg, the principle of which is the administration of massive doses of x-rays in the shortest possible time commensurate with safety as regards the skin of the areas irradiated.

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[1] Lancet, 1921, **200**, 309.

In a few cases the total dose has been reduced by diminishing the number of areas irradiated at each sitting and it is noteworthy that the cases so treated comprise the greater proportion of failures in the series. They frequently showed a recurrence of the hemorrhage after a varying period of amenorrhea so that they have come to the conclusion that the two most important points in the treatment are the giving of massive doses and the administration of the treatment for one or two doses after amenorrhea has been produced. They have succeeded in all but 5 cases treated by x-rays either in inducing complete amenorrhea or in so reducing the frequency and severity of the losses as to relieve symptoms completely. The dose required, as estimated by the time exposure, varied very much, the limits being two hours and twenty-seven minutes and fifteen hours and thirty-five minutes. The longest exposures (those over ten hours) were all given in cases of fibroid tumors, and on an average it may be said that cases of chronic metritis require a smaller dose to produce amenorrhea than do fibroids. They do not find that the age of the patient has any bearing on the size of the dose required although they had anticipated that the younger patients would require the larger doses.

They have taken the symptom of "flushings" as the best available guide to the severity of the menopausal effects and inquiry has been made upon this head in every case. The result is that in a little less than 50 per cent of their cases "flushings" have been reported as slight or absent, in one-eighth they were reported as moderate, and in three-eighths as severe. In many of the latter class the flushings were frequent both day and night and persisted in some for two years or more after the treatment had ceased and they are of the impression that in some of the cases, a small proportion of the whole, this symptom was more severe and prolonged than they have ever noticed it in the natural climacteric. In all other respects there is nothing that calls for comment in the menopause, except that nervous symptoms of a functional character appeared to be less frequent than under natural conditions. Although the majority have gained a certain amount of weight after the treatment, there has been no tendency to corpulence of an unsightly character and there has not been a single instance in which signs of masculinity appeared, nor has there been any loss of sexual feeling.

Inasmuch as x-ray treatment is only suitable for carefully selected cases, they do not think that it will ever supplant hysterectomy as the chief method of dealing with cases of uncontrollable uterine hemorrhage. To many women an operation is an ordeal which is greatly dreaded and in certain others, special conditions which increase operative risks, such as Graves' disease or valvular disease of the heart, make roentgen therapy a welcome substitute for operation. As a rule, in cases suitable for x-ray treatment, Eden and Provis allow the patient to decide whether she will be operated upon or whether she will be treated by the rays, unless some complication exists which will increase the operative risk. As compared with hysterectomy, x-ray treatment has the advantages that the ordinary life and work of the patient need not be interrupted for more than two days at a time, and that the prolonged partial invalid-

ism, which often lasts for several months after an abdominal operation, is completely avoided. The disadvantages of the x-ray treatment are the uncertainty as to the length of time required to produce the result aimed at, and the very slight risk there may be that the treatment will be successful and that operation may be eventually required. The latter is a minimal risk and will no doubt be eliminated entirely as experience grows.

Having reviewed at length the foregoing report of well-known British surgeons, it might be of interest to direct our attention for a moment to the opinion of an American investigator. Kinney[1] very wisely remarks that uterine hemorrhage is a presenting symptom, never a diagnosis, and the underlying pathology must be ascertained before any intelligent treatment can be instituted. In approaching a case of prolonged atypical hemorrhage, one must eliminate, first, the accidents and incidents of pregnancy, second, pelvic infection and, third, malignancy. Having ruled out this triad, practically every case of uterine hemorrhage can be controlled by roentgenotherapy. However, efficient x-ray treatment involves the establishment of the menopause and sterility, and therefore the x-ray will only be called into use after the general physical and mechanical conditions have been ruled out or properly treated. There are cases on record where the ovaries have been protected during x-ray treatment and normal menstruation and normal pregnancy have followed a clinical cure. However, the danger of the complete arrest of menstruation limits the x-ray treatment of uterine hemorrhage to those conditions where the establishment of the menopause is justifiable. Kinney has found roentgenotherapy efficient and suitable in the following types of cases:

1. In patients that have atypical bleeding from a grossly normal uterus nearing the menopause. The hemorrhage can be controlled and the menopause established in 100 per cent of these cases.

2. In uterine hemorrhage from small fibroids at or near the menopause, the arrest of the bleeding and the establishment of the menopause are certain, and the fibroid will disappear or decrease in size and become symptomless.

3. Patients that are poor surgical risks with uterine hemorrhage from any type of fibroid can be relieved from their symptoms of hemorrhage quickly and effectually by x-ray.

4. There are certain cases where uterine hemorrhage and dysmenorrhea are so destroying the patient's emotional and mental balance or so undermining her physical condition that a menopause is justifiable, and where it is justifiable it can be secured easily and certainly with roentgenotherapy.

On the other hand, roentgenotherapy is contraindicated where the establishment of a menopause is not justifiable, and is contraindicated in the treatment of uterine hemorrhage where that hemorrhage is a symptom of an urgent surgical condition. Uterine hemorrhage in adolescence can be readily controlled without danger by radium and it is

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[1] California State Journal of Medicine, 1921, **19**, 76.

not justifiable to assume the risk of the menopause except where radium is not obtainable or in extreme cases. In the hemorrhage of uterine fibroids in young women, the patients should be given the chance of myomectomy, if possible, rather than hazard their expectancy of motherhood. Uterine hemorrhage accompanying a submucous or sloughing fibroid is the presenting symptom of a distinctly surgical condition and should only be treated as such. The treatment of large fibroids with symptoms of pressure can be successfully carried out with x-rays and is justifiable in those cases presenting serious surgical counterindications, but whether the roentgen treatment of patients with large fibroids that are good surgical risks is justifiable is still an open question. Kinney does not believe that it is justifiable and considers that the extirpation should be strongly advised for every patient having a large fibroid or with definite pressure symptoms. Furthermore, uterine hemorrhage with malignancy is an indication for either radium or surgery, and one must be constantly on guard to see that these cases have their radium or their surgery at the earliest possible moment. The foregoing statements and opinions are as fair and as unbiased as we have ever known to come from a roentgenologist.

Operative Treatment of Myoma Uteri. The conscientious and thoughtful operator makes every effort to preserve the menstrual function of his patient when dealing with fibroid tumors of the uterus. Vineberg[1] insists upon the importance of preservation of the menstrual function, for the ovaries, to his mind, serve no useful purpose when the uterus has been removed or when the endometrium has been destroyed so that menstruation is no longer possible. Some of the very worst cases of the artificial menopause syndrome have been witnessed in women who had their ovaries and their uterus *in situ*, but in whom a too energetic curettage had brought about a permanent cessation of menstruation. The same applies to instances where the uterus was removed and the ovaries left behind, says Vineberg. There is to be observed at the present time a singular state of mind on the part of the medical men who are all keenly alive to the importance of preserving the menstrual function in women. They hesitate to consign their patients to an operation which would destroy that function, still they refer without a moment's hesitation, a patient with a bleeding fibroid of the uterus to a roentgenologist or radiologist, who can only be successful in destroying that function, and in most instances, permanently. Every patient who consults Vineberg regarding a fibroid tumor causing symptoms, is told that she may have her choice of treatment, either by operation, or by x-ray or radium. He tells her, regardless of her age, that the one (operation) perhaps carries more risk with it than do the others, but that in his opinion it is a more certain permanent cure. If she is under forty, he tries to impress her with the advantages, of which he is strongly convinced, of submitting to an operation, the endeavor of which would be to remove her tumor or tumors, and preserve her menstrual function. In spite of strongest determination and painstaking efforts, it must be

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[1] Medical Record, 1921, **99**, 91.

admitted that cases will be encountered now and then in which it is not possible to save the uterus. What we must endeavor to do then is to save enough of the organ and endometrium to carry on the function of menstruation. Even should we be baffled in this and the entire organ have to be sacrificed, the patient would in no wise be any worse regarding her menstrual function than she would have been had she been success-fully treated with *x*-ray or radium. On the contrary, Vineberg believes she would be better off, for her cure would be more certain and more complete.

Taussig[1] brings up a point which has thus far not received the atten-tion of most surgeons and statisticians. While he believes that radio-therapy of fibroid tumors is destined more and more to displace operation as patients learn to come early before contraindications to its use have arisen, in the negress he believes that surgery will still have to be generally employed in fibroid tumors on account of their earlier, more rapid, and more complicated development. In his experience, only 7.3 per cent of negro patients with fibroids were suitable for radium, as opposed to 56 per cent of the white patients.

Hornung[2] reports the results of 447 operations for myoma, 25 per cent of which were performed on nulliparæ. The chief symptoms were pain and hemorrhage. In some cases there were urinary symptoms consisting of a feeling of pressure on the bladder or of traction on its neck. In 47 cases there were complicating tumors of the adnexa, in 31 cystomata; in 2, adenocarcinoma of both ovaries. Sarcomatous de-generation was present in 2 per cent of the cases. In 5 cases there was also carcinoma of the body of the uterus, and in 2 cases carcinoma of the cervix. Six patients were pregnant and in 2 cases there was tubal pregnancy. The total mortality was 8 deaths (1.79 per cent). Embol-ism of the lung occurred on the fourth, ninth and tenth days respectively in 3 cases which were progressing uneventfully up to that time. One patient died of ileus, 1 of toxemia and 3 of sepsis. The adnexa on both sides were removed in 210 cases, on one side in 79 cases. In 4 enuclea-tions of the pregnant uterus, abortion occurred in only 1. In 1 case an injured ureter was implanted in the bladder, with an uneventful recovery. In 9 cases recovery was complicated by respiratory disease, in 4 by cystitis and in 4 by hematoma. He believes that women who have bled a great deal should be operated upon by the vaginal route if possible. The size of the tumor is not the deciding factor but rather its mobility and the possibility of bringing it down in the pelvis. In 175 vaginal operations, Schuchardt's incision was necessary in only 29 cases.

Embolism after Hysterectomy for Myoma. A patient has had a hysterec-tomy for a uterine myoma and has had a satisfactory recovery and is about to be allowed out of bed, the family having been assured that complete recovery is merely a matter of time, when suddenly, the patient collapses and death ensues in less time than it takes to describe. Such is the sad picture of pulmonary embolism as it occurs in a small per-centage of cases following pelvic operations, and we stand helplessly

[1] Journal of the American Medical Association, 1921, **77**, 357.
[2] Zentralbl. f. Gyn., 1921, **45**, 381, by International Abstract Surgery.

by when the condition occurs, realizing that our efforts are futile. Any investigation which would reduce the incidence of such a dreaded complication would undoubtedly receive recognition from the profession and therefore we desire the reader to become acquainted with the work of Farrar[1] based on observations in the Woman's Hospital in New York. She finds that pulmonary embolism or thrombosis is the most frequent cause of postoperative pulmonary complications following hysterectomy for myoma uteri, and the source of the embolism is a thrombosis of the pelvic veins or the veins of the lower extremities, or a thrombosis of the right heart. The development of a thrombosis or an embolism may be during an operation or immediately following it. The most frequent time seems to be during the first forty-eight hours. The symptoms in the order of their most frequent occurrence are pain, friction rub, cough, bloody sputum and rales, dulness and alteration of breath sounds. These signs are premonitory of a thrombosis, but the evidences of thrombosis of the veins of the lower extremity or pelvic veins do not appear until later. The physical findings at the onset are similar to lobar pneumonia or pleurisy, but the clinical picture soon separates the cases. In differential diagnosis the roentgen ray may be of value. The causes of thrombosis are (1) an enfeebled circulation due to (a) dilated venous trunks, especially of the pelvis and lower extremities, (b) venous stasis, (c) lowered blood volume due to hemorrhage or shock, (d) myocardial insufficiency, and (2) infection. The treatment of this condition should be prophylactic and directed to improving the circulation of the blood by strengthening the heart muscles and walls of the bloodvessels and increasing the hemoglobin of the blood. The importance of rest in bed as a preliminary to operation to relieve the pressure of large myomata on the veins of the pelvis and lower extremities, the use of blood transfusion *before* operation in cases of marked anemia and the maintainence of blood volume during operation by gum glucose solution given intravenously, should be emphasized. In substantiating this theory, Farrar reports that during a two-year period all ward patients having large fibroids were kept in bed from five to seven days prior to operation, and no embolism or thrombosis occurred in any case. In the private patients, who were not kept in bed prior to operation, a fatal embolism occurred once and venous thrombosis six times during the same period with exactly the same operative technic.

Intraperitoneal Hemorrhage from Myoma. It is customary to regard uterine fibroids as benign tumors, insofar as acute life-threatening complications are concerned. The operative cure is, as a rule, one of choice, undertaken because of the size of the tumor, pressure symptoms, bleeding or malignancy. Intra-abdominal hemorrhage from one of these tumors is indeed a rare complication and is usually due to rupture of one or more dilated superficial veins, just beneath the peritoneum. Such a case has been reported by Ransohoff and Dreyfoos[2] who state that the clinical picture was that of an acute abdominal emergency and their diagnosis was that of a twisted ovarian cyst. Upon opening the

[1] American Journal of Obstetrics and Gynecology, 1921, **2**, 286.
[2] Surgery, Gynecology and Obstetrics, 1921, **33**, 296.

abdomen, about two liters of free blood was found in the abdominal cavity and the bleeding was seen to come from two ruptured varicose veins on the anterior surface of the fibroid. In spite of the severity of the condition, the patient made an uneventful postoperative recovery. They caution that if the patient is in a desperate condition, instead of performing a hysterectomy, it would be a more simple matter to transfix and ligate the bleeding vein on either side of the opening, and do a hysterectomy at some future date, after the recovery of the patient from the effects of the hemorrhage.

Disposition of the Ovaries in Hysterectomy. As a result of a careful follow-up investigation on 84 patients who had been operated upon for uterine fibroids, Hawks[1] has come to the conclusion that the onset of the vasomotor disturbance is delayed when one ovary is left and further delayed when both ovaries are left. Very little serious harm was caused by a retained ovary. One patient among 65 was referred for a secondary operation on account of a cyst. Twelve among 65 complained of pain or had a swelling at the site of a retained ovary, but in 11 of the 12 the trouble disappeared after about three months. There was more trouble when the tube was removed than when it was left with the ovary.

Fibromyoma of the Abdominal Wall Following Hysterectomy. The object of a communication by Brewer[2] is to report and place on record the history of a patient in which a large, typical, fibromyomatous tumor developed in the abdominal wall, in the scar of a previous laparotomy undertaken for the removal of a uterus, which was the seat of multiple growths of the same character. To account for the development of this tumor in this unusual location, he considers only four possibilities: First, that it arose spontaneously from the subperitoneal connective tissue; second, that it developed from the urachus; third, that it was of teratomatous origin; and fourth, that it was an implantation tumor originating from some minute fragment of the primary tumor left in the abdominal incision at the time of the previous operation. He has been unable to find a report of a single case of a typical fibromyoma of the abdominal wall and, similarly, has been unable to discover an authentic instance of a tumor of this variety arising from areolar or fatty tissues in any part of the body, and no record has been found of a fibromyoma developing from the urachus, whether patent or obliterated.

These facts and the recognized impossibility of leiomyomatous tumors developing from tissues containing no smooth or unstriated muscular fibers excludes the first hypothesis that such a neoplasm could spontaneously develop in the subperitoneal areolar or fatty layer of the abdominal wall.

In regard to the urachal origin of the growth, the absence of any recorded example of a fibromyoma arising from this structure, and the absence of any evidence in this case of an attachment to anything resembling the urachal cord, would render the second possibility highly improbable.

In regard to the third, or teratomatous origin of the tumor, it must be

[1] American Journal of Obstetrics and Gynecology, 1921, **1**, 959.
[2] Annals of Surgery, 1921, **74**, 364.

admitted that the median line of the abdomen is a well recognized habitat for these minute islands of embryonal tissue and numerous example of teratomatous growths from these rests have been recorded. In all such cases however, that have been carefully examined, although one type of tissue may preponderate and make up the great mass of the tumor, a painstaking search will always reveal the presence of other types of tissue in some part of the neoplasm. The absence in this instance of any evidence of the presence of other types of embryonal tissue would lead one logically to exclude this explanation of its origin.

In regard to the fourth hypothesis, that it arose from the implantation in the line of the incision of a minute fragment of the uterine tumor removed ten years before, Brewer is of the opinion that this is by far the most probable and reasonable explanation of its occurrence. This opinion is based upon the following facts: First, the coincidence of the development of this tumor in an individual who had previously harbored an exactly similar growth in a neighboring structure; second, that in its removal the tumor-bearing organ with its divided and exposed tissues had been for some time in actual physical contact with the divided and exposed tissues of the abdominal wall, in the exact location in which the secondary growth subsequently developed; third, the well-known and generally recognized fact, that certain cutaneous and mucous membrane tumors which are in close or frequent contact with neighboring tissues not infrequently give rise to similar growths in the tissues thus exposed; fourth, that modern experimental surgery has furnished innumerable examples of successful grafts of tumor tissue as well as normal glandular structures in both animal and man; and fifth, that surgical literature records not a few examples of both benign and malignant tumors arising in the immediate neighborhood of incisions previously made for the removal of histologically similar growths.

New Uterine Suspension Operation. A review of gynecologic literature for any given year would not be complete if mention were not made of at least one of the dozen or so new operations for suspension of the uterus which are thrust upon the profession every year. One of these new operations has been described by Grad[1] and consists of a subperitoneal shortening of the round ligaments. He has performed several hundred of these operations during a period of eight years and, from a review of 100 cases in which a follow-up study was made, he is convinced that his operation eclipses all its predecessors. Such a feeling, however, is rather common among inventors of operations. In brief, the technic of the operation consists of grasping the round ligament midway between its cornual insertion and the internal ring and putting the ligament on tension. Immediately below the grasp of the forceps, the operator picks up the anterior layer of the broad ligament with a thumb forceps and nicks it with a scissors. Beginning at this point, with the scissors, the incision in the anterior layer of the broad ligament is extended, along the edge of the round ligament, until the internal ring of the inguinal canal is reached. In this manner, the entire round ligament is

divested of its peritoneum and the broad ligaments are separated. A stitch of linen is then taken in the pillars of the ring which also picks up half of the round ligament as it enters the ring and then, with the same suture, the round ligament is picked up, inside of its denuded area, about one inch from its uterine end and the two points of the ligament are brought together by tying the suture. The uterine end of the ligament is then sutured to the pillars of the internal ring with a few linen sutures and the intervening redundant portion of the round ligament is sutured together and then buried between the layers of the broad ligament, all of this being accomplished with the original suture. The anterior
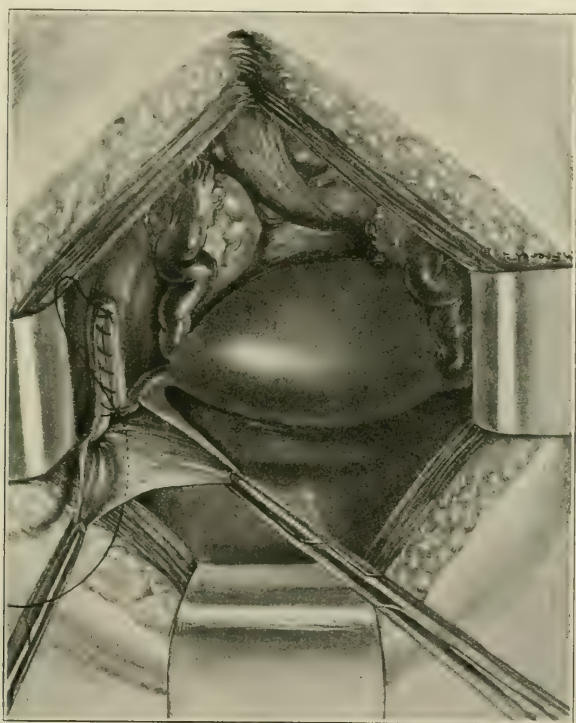
Fig. 2.—Technic of operation. (Grad.)

layer of the broad ligament is then sutured with catgut to the posterior surface of the round ligament, burying the redundant round ligament and covering all raw surfaces. After the procedure is performed on both sides, the operation is frequently supplemented by performing a shortening of the utero-sacral ligaments or by a ventro-suspension by means of a single catgut stitch, so as to be only temporary in nature. As a result of Grad's investigation into this subject, he concludes that every case of retroversion of the uterus with symptoms requires an abdominal section and, for this purpose, the above operation is readily performed and is not time-consuming, creates no abnormal conditions in the pelvis, tunnels no holes through the abdominal parietes, causes no

intraperitoneal complications, does not interfere with pregnancy or labor, is devoid of mortality and morbidity and the final results of the operation show 95 per cent of successes which should be a very high recommendation.

The Stem Pessary. The stem pessary is up again for discussion after a peaceful slumber for a few years. This time Rawls[1] has studied the end-results in 117 cases in which a stem pessary was used for one reason or another in the Woman's Hospital in New York and has come to fairly definite conclusions. He states that the intra-uterine stem pessary has a limited field of usefulness in gynecology. It is applicable to 51.7 per cent of cases suffering either from dysmenorrhea, sterility, amenorrhea, anteflexion of the uterus, stenosis of the cervix, or congenital malformation of the uterus. As an operative measure it is applicable to 2.3 per cent of patients treated, and 1.3 per cent of operations performed in a gynecological ward. From its use, sequelæ, other than a temporary rise of temperature, occur in from 17.6 per cent to 21.8 per cent of the cases, with a permanent morbidity of from 5.8 per cent to 9.8 per cent. As a therapeutic measure for dysmenorrhea, there is improvement in 77.8 per cent, with relief in 61.1 per cent and for sterility there is relief in 23.4 per cent. The intra-uterine stem pessary gives as good end-results as other operative procedures for like indications and from its use there is less primary invalidism and no more liability to sequelæ or morbidity. The stem pessary should never be used except in carefully studied and selected cases and then the minimum of sequelæ and morbidity with the maximum of result will be obtained as evidenced by the careful study which Rawls has made.

Action of the Emmenagogue Oils on the Uterus. Some experiments which have been performed on the isolated human uterus by Gunn[2] to determine the action of emmenagogue oils agree with the results of other observers on the excised uterus of other mammalia. It would seem that the emmenagogue oils in very small amounts have no action at all on the uterus. In higher concentrations, such as could never be reached in the blood without producing dangerous, probably fatal, poisoning, they inhibit uterine movements. When abortion occurs after their use, it is probably an indirect result of severe inflammation and irritation of the bowel and kidneys. This may induce congestion and reflex movements of the uterus which may, in some cases, result in abortion. The absence of specific stimulant action of these oils on the uterus renders them all the more dangerous poisons, as, after their failure in ordinary doses, large ones are sometimes taken, resulting in frequent poisoning, in a large proportion of cases without the production of abortion.

Gynecologic Backache. A small volume might be written about backache if this symptom were studied exhaustedly from every viewpoint, and a most interesting and instructive treatise it would be. Probably the longest chapter should be written by the orthopedist, but the gynecologist, neurologist and internist could contribute much interesting

[1] American Journal of Obstetrics and Gynecology, 1921, **1**, 499.
[2] Journal of Pharmacology and Experimental Therapeutics, 1921, **16**, 485.

material, and so interdependent should these be that the authors would do well to consult each other freely in the preparation of the work. Some surprising observations made in the postoperative follow-up clinic at the Woman's Hospital in New York during the past few years led Bullard[1] to feel that an analytical study of backache would be interesting. As a result of such an investigation, he found that in a series of 721 cases of backache studied, 85 per cent were cured by an appropriate operation. About 15 per cent of this series presenting one or more common gynecological causes of backache were not relieved of the backache by anatomically satisfactory operations. Probably much more than 15 per cent of the backache in females is not gynecological. This study suggests that 15 to 20 per cent of all women with retroversion, prolapse, pelvic inflammation, obstetrical lacerations, or pelvic tumors, do not have backache. Closer coöperation with the orthopedist, internist and neurologist should enable the gynecologists better to diagnose and treat backache in women.

Pneumoperitoneum in Gynecologic Diagnosis. Peterson[2] is most enthusiastic over the aid he has obtained in making diagnoses in pelvic cases by the use of carbon dioxide inflation of the pelvic cavity followed by roentgenographic examination. The pelvis has been inflated with gas in over 150 cases with no reaction which could be attributable to the gas itself or to the method employed. It goes without saying that modern surgical methods of sterilization must be employed, but this is true when we introduce a uterine sound or perform abdominal paracentesis. Actual experience and animal experimentation have shown that there is no danger of injuring the intestines by the needle thrust through the abdominal wall where the intestines are not adherent to the parietes. Where the puncture is made in the presence of adhesions, a locality should be selected which is free from adherent gut.

Very rarely will a patient be found who will suffer no discomfort from the injection of enough gas into the abdominal cavity to insure a satisfactory roentgenogram. The discomfort is not connected with the passage of the needle, for this can be rendered practically painless by means of local anesthesia. The discomfort is caused by the rapid distention of the peritoneal cavity and the more gas injected, the greater the discomfort, hence our efforts should be directed to elaborating a technic which will give a good pelvic picture with a minimum amount of gas. The average patient will begin to complain of discomfort about the lower abdomen when 400 to 500 cubic centimeters of gas have been introduced and it is rarely necessary to inject more than 1000 cubic centimeters. Discomfort is increased by the rapid injection of gas, and there is always a tendency to inflate the patient more quickly than is necessary. This tendency should be controlled if we are to reduce discomfort to a minimum. Carbon dioxide gas is preferred over oxygen because it is absorbed in fifteen to twenty minutes, with a prompt cessation of pain, so that a patient can walk in a half hour after the examination. When oxygen was used, patients sometimes suffered for hours

[1] New York Medical Journal, 1921, 113, 142.
[2] Surgery, Gynecology and Obstetrics, 1921, **33**, 154.

unless the gas was removed by another abdominal puncture. To insure successful pelvic roentgenography, the patient must be so placed as to allow of the gas rising upward and displacing the pelvic organs and forcing the intestinal coils out of the pelvis. After many trials with different positions, Peterson is securing the best results with a moderate knee-chest position with an inclined board beneath the thighs with a notch cut out for the tubes. The table is then tipped as for the Trendelenburg position, the patient being prevented from slipping by shoulder straps. The uterus, tubes and ovaries, together with almost any pathology that may be present, can usually be easily demonstrated on the plates made according to this technic.

THE FALLOPIAN TUBES.

Ectopic Pregnancy. Any series of 307 cases of ectopic pregnancy must be of interest to the gynecologist, but when, in addition to its size, such a series occurs in the practice of and is analyzed by such a surgeon as Polak[1] it must of necessity contain much of practical importance. His experience has shown that, clinically, all ectopics fall into two general classes: (1) Those which may be classified as in the non-tragic stage, with a pulse distinctly countable of 100 or under, with a systolic pressure of 100 or over and a hemoglobin of 60 per cent or more. In this class there were 263 cases. (2) Those in the tragic stage, pulseless at the wrist, with a blood pressure below 90, a hemoglobin under 50 and definite signs of internal hemorrhage and collapse. In this class there were 36 cases. The analysis of this series shows that ectopic pregnancy occurs most frequently where there is a congenital anomaly or a previous inflammation of the tube, in the woman who gives a history of premenstrual dysmenorrhea. Like other pregnancies there is a period of amenorrhea or an attempt at menstrual suppression, but because of the unstable position of the ovum owing to the imperfectly developed tubal decidua and erosion of the ovum into the underlying muscle and venous radicles, bleeding takes place into the decidua and produces such ovular unrest as to cause tubal distention and peristalsis which is evidenced by colicky pains and uterine bleeding. The bleeding into the decidua plus the growing ovum distends the tube and causes the soreness and tenderness over the region of the distended gestation sac.

The relation of the physical signs to the pathology is still more striking and constant as was shown by a study of this series. The uterus is enlarged, because it contains a decidua which was prepared in anticipation for the reception of an ovum. This sign could be definitely demonstrated in all of the ectopic pregnancies of eight weeks or over. The cervix is soft due to the congestion incident to pregnancy. This symptom is variable and is of no diagnostic importance and was noted in a very few of the cases. Bimanual examination shows that the uterus does not have the usual characteristic diagnostic sign of pregnancy, *i. e.,* the elasticity of the median portion of the anterior wall and the

[1] American Journal of Obstetrics and Gynecology, 1921, **2,** 280.

compressibility of its isthmus. The absence of these changes in consistency is due to the absence of the growing ovum in the uterus, which, though it is enlarged, is not changed in shape or consistency except for the slight softening of the cervix which is not constantly present. The cervix is exquisitely sensitive to motion. This is shown by palpation and is due to the peritoneal irritation from the blood which gravitates from the end of the tube or through the tubal wall because of its porosity and finally to the prolapse of the tubal mass into the cul-de-sac. This reaction of the peritoneum covering the utero-sacral ligaments makes them sensitive, hence anything which moves these sensitive bands will cause exquisite pain. This sign, pain on movement of the cervix, was present in all of the cases in this series. In considering the proper treatment of ectopic pregnancy, it should be remembered that primary rupture of the tube is not usually serious nor fatal. Less than 1 per cent bleed to death, 3 out of 307 cases in this series from the primary rupture, as the usual erosion goes through an arterial twig, and not the main vessel. Bleeding continues until the blood pressure falls, a clot forms and the bleeding ceases. The patient reacts, feels well for a day or two, and then a secondary rupture occurs and the doctor who has treated her for indigestion has missed the psychological moment to do the operation in the non-tragic stage. Polak's experience teaches him that the best time to operate is after a reaction. This is shown by the slower pulse and gradual increase of blood pressure. Almost all of these patients will come back with rest and morphine. He gives them an initial dose of $\frac{1}{2}$ grain and $\frac{1}{4}$ grain every three hours, reducing the respirations to eight or twelve, and he has yet to see a case which has not reacted and become a safe operable risk under this treatment. No saline is used until after the operation, then never by infusion. Blood transfusion is preferable when the vessel has been tied, never before, but it is indicated during the procedure in severe cases. The operation consists in properly removing the tube without interfering with the collateral circulation of the ovary. This can only be done by individual ligation of the vessels in the mesosalpinx, not by mass ligature. After the tube is removed, the ovary is suspended by suture of the infundibulo-pelvic ligament to the round ligament and the raw surface at the top of the broad ligament peritonealized by whipping the mesosalpinx and round ligament together. It is only possible by waiting for reaction from shock to select the time for operation, then we can give the woman her best chance both as to mortality and morbidity.

Autotransfusion in Ectopic Pregnancy. In a series of 34 cases of ectopic gestation which were operated upon for rupture with hemorrhage, Schweitzer[1] reinfused the patient's own blood in 21 cases and found this to be a useful, and in many cases, a life-saving procedure. It is free from danger when it is free from infection, when there are no blood clots and the blood cells are in an intact condition. One patient died from hemoglobinuria. If it should be discovered that hemoglobinuria cannot be prevented, the harmlessness of this procedure will be doubtful.

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[1] München. med. Wchnschr., 1921, **68**, 699.

Although other investigators have reported such disturbances as cyanosis, dyspnea, pains in the thorax, convulsions and chills after this procedure, no permanent injuries nor deaths have been reported heretofore.

Non-gestational Tubal Hemorrhage. Hemorrhage into the abdominal cavity from an ovary or Fallopian tube is so generally due to the terminal changes in an ectopic ovum that the recognition of other causes for the bleeding has been rather neglected, states Schumann[1] even though such other causes are known to exist. The preoperative differentiation from hemorrhage due to ectopic pregnancy is rarely possible save in those cases in which the virginity of the patient is beyond all question. The symptomatology and the clinical picture are simply characteristic of sudden intraperitoneal hemorrhage, more or less in amount, and usually associated with acute pain in one or the other iliac fossa, although in a few cases the initial pain is entirely absent, distress only becoming apparent when the irritating effect of the free blood in the peritoneal cavity produces its usually dull, generalized, abdominal ache. There follows usually some distention, with signs of shock and severe blood loss, or the sthenic reaction of elevation of temperature, moderate leukocytosis, rectus rigidity, and, in general, the syndrome of the "acute abdomen." The important point in the preoperative diagnosis is that from the personal as well as from the medico-legal standpoint, a diagnosis of ectopic pregnancy should not be made in cases in which pregnancy should not exist. Schumann agrees with Bovee who believes that in the presence of hemorrhage of tubal or ovarian origin, when there is not positive clinical evidence of pregnancy as evidenced by the finding of a fetus or chorionic villi, one is not justified in making a diagnosis of extrauterine pregnancy, unless proved by microscopic examination. The one group of cases of this sort wherein a preoperative diagnosis may be hazarded is that fairly common one in which growing girls, during one of their early menstrual periods, display all of the phenomena of intraperitoneal hemorrhage. It is probable that such ovarian hemorrhages are more or less functional errors, that is, an excess of bleeding from the wall of the mature Graafian follicle in the adolescent ovary, and that there is no demonstrable morphologic change present in the tissues. The type of case that gives rise to the greatest confusion is that in which more or less severe hemorrhage takes place from the ovary of mature women and in which the occurrence of extra-uterine pregnancy is a possibility. Here the preoperative diagnosis is extremely difficult, although the history is sometimes suggestive, in that there has been nothing unusual noted with regard to the menstrual cycle and especially in that there is no associated uterine bleeding.

Unusual Pregnancy After Ectopic Gestation. Shaw[2] reports a case in which, by means of a rather unusual operative procedure, the possibility of conception was preserved in a case in which at a previous operation the right tube and ovary had been removed and in which at the second operation a cornual pregnancy was found on the left side. Cullen, who operated, laid the outer part of the left tube carefully aside, and, after

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[1] Journal of the American Medical Association, 1921, **77**, 692.
[2] Bulletin of the Johns Hopkins Hospital, 1921, **32**, 305.

removing the cornu, inserted the proximal portion of the remaining portion of the left tube into the uterine cavity. Pregnancy followed.

Surgical Treatment of Chronic Tubal Infections. The rule followed by Blair Bell[1] in deciding when to operate upon chronic tubal infections is that, if a patient whose temperature has been absolutely normal for some time shows any degree of pyrexia on the evening or day following vaginal or rectal examination, an eradicative operation must not be performed. The patient must be able to stand handling without showing any reaction before such an operation is safe. This is of most importance, of course, when we are dealing with lesions primarily due to streptococcus infections; but, as other infections, especially gonococcal, may be complicated by streptococcal invasion, this test should always be applied. The streptococcus, unlike the gonococcus, does not usually lead to the destruction of the lining membranes of the uterus and Fallopian tubes. This organism tends, rather, to pass through the mucosa to reach the lymphatics. Abscesses may, however, result from an acute infection in the uterus, tubes and ovaries, but in his experience abscesses in the uterus and tubes require intervention before they can become chronic, whereas abscesses in the ovaries may be encountered in a quiescent state. The chronic lesions then, may consist of chronic metritis as a separate pathologic entity, or of salpingitis, with the production of a hydrosalpinx or a sealed abdominal ostium, either alone or associated with an ovarian abscess. Such infections are often limited to the appendages of one side. When the lesion is unilateral it is necessary to remove only the tube and ovary of the affected side, if no conservative operation, such as salpingostomy is indicated. If both tubes are occluded but not distended, and at least one ovary appears to be little affected, then salpingostomy on one or on both tubes should be practised. It is useless to perform salpingostomy on a hydrosalpinx, for the uterine end of the tube is blocked. If both ovaries contain abscesses they must be removed, and a portion of one must be grafted. If this is necessary, conservative operations on the tubes are, of course, unnecessary. The functional results of salpingostomy cannot yet be stated with certainty so far as Bell's cases are concerned, but the fact that conception does occasionally follow this procedure encouraged him to hope that with improvements in technic it will more often be successful. Moreover, it is consoling to the patient to know that there is a possibility, however remote, of subsequent pregnancy.

In considering tuberculous infection of the tubes, which is unfortunately common in the young adults, Bell states that the tubes must be removed when the peritoneal fluid is evacuated, and it is wise to remove the uterine cornua at the same time. The ovaries are unaffected, as a rule, by an infection reaching them from without, that is, from the peritoneum, hence it is usually safe to leave one of them if it should show no obvious lesion, or to graft a portion of it.

In sexually active women who are afflicted with gonococcus infection, when the fundus uteri and appendages are attacked, he performs the

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[1] Journal of the American Medical Association, 1921, **77**, 696.

operation which he described some years ago, in which he excises in one piece the tubes, ovaries and a transverse wedge-shaped portion of the fundus uteri. He has performed this operation 125 times with the loss of only 2 patients, 1 of whom died from an intercurrent affection.

Bacteriology and Pathology of Tubes Removed at Operation. A very interesting investigation into the bacteriology and pathology of Fallopian tubes removed at operation has been conducted by Curtis.[1] The diseased tissues from 192 cases were placed in sterile towels immediately upon removal from the abdomen. Smears were made and all except portions saved for histologic examination were thoroughly ground and the entire material was inoculated into culture media. A considerable variety of media was used. Meat-infusion-ascites-blood-agar, under partial oxygen tension, yielded most uniform success in the cultivation of the gonococcus. For convenience in study, these patients were arranged in three groups; those with grossly active inflammation, those with inflammation demonstrable only upon microscopic examination, and those without definite evidence of an active process. Cultures were positive in 38 cases, as follows: gonococcus 19, non-hemolytic streptococcus 6, hemolytic streptococcus 3, anaërobic streptococcus 5, bacillus coli 3, mixed infection 3, bacillus proteus 1, while 9 revealed tuberculosis. In the material so studied it has never been possible to obtain gonococci from patients who failed to reveal gross evidence of active inflammation at the time of operation. It has heretofore been impossible to form a definite clinical estimate of the length of time which the gonococcus remains viable in the Fallopian tubes; this is particularly true of those cases in which patients give evidence of recurrently active or persistent tubal disease. It has long been known that gonococci soon disappear from the tubal mucosa, but proof that infection does not persist in the deeper tubal structures has been wanting. Whether the gonococcus produces a chronic salpingitis or these patients suffer from repeated gonorrhea of the tubes seems to Curtis to be an important issue. It is therefore of interest to note that in this work, in all of which cases the Fallopian tubes were ground and promptly cultured according to approved modern methods, it has rarely been possible to obtain viable gonococci from patients who have been free from fever and leukocytosis for a period of more than ten days or two weeks. The fact that good growth was obtained in more recent tubal infections is evidence of satisfactory cultural methods. In view of the many cases studied in this way, Curtis feels warranted in the deduction that the gonococcus lives but a short time in the tube; in other words, it seems that the Fallopian tube is not to be regarded as a focus of chronic gonorrheal infection. Persistently active gonorrhea of the tubes is evidently ascribable either to recurrence of infection from without or repeated invasion of the bacteria from the chronically infected lower genital tract.

Not only in the non-hemolytic group, but also with infections with other types of streptococci, pathologic evidence of an active inflammatory process was sometimes encountered long subsequent to the

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[1] Surgery, Gynecology and Obstetrics, 1921, **33**, 621.

introduction of the infection, in contradistinction to the gonorrheal group. Furthermore, bacteria were more persistent than the pathologic evidence would indicate. Streptococci were occasionally isolated in pure culture many months, or even years, after the acute process had subsided.

From the clinical history, examination of the external genitalia, and evidence obtained at operation, together with laboratory study of the tubes in this series of nearly 300 patients, it has been possible to determine that gonococcal infection was responsible for the pathologic condition in more than 70 per cent of the cases. Approximately 10 per cent more were thought to have been primarily infected with the gonococcus, but this could not be determined with certainty. It has been particularly noted that a single attack of salpingitis seldom results in marked permanent increase in thickness of the tubal wall. Greatly thickened tubes are most often associated with repeated exposures. If the patient can be early isolated from the source of her infection, there is reason to expect moderate tubal changes. Only occasionally are gonococci sufficiently virulent to make an exception to this general rule. Persistent pyosalpinx exemplifies gonorrheal infection in severe form, and is particularly characterized by hyperplasia and induration of the tube wall. In a lesser measure the same holds true for the tubal changes in hydrosalpinx. The belief that hydrosalpinx and pyosalpinx are fundamentally different lesions has not been borne out by this study. A comparison of histologic material reveals innumerable gradations from one to the other. In greatly thickened old tubes, bloodvessels are very numerous. Aside from recognized tubal pregnancy, none of which cases were wittingly included, there were studied more than half a dozen such tubes with rich blood supply in which there was extensive hemorrhage within the tube lumen. By means of serial sections it was possible to demonstrate the site of bloodvessel rupture in one case. The question arises whether we have not placed too much reliance upon hematosalpinx as a dependable evidence of tubal gestation. Possibility of this error is increased by the fact that microscopic examination of these blood-filled, greatly thickened tubes reveals an overgrowth of distorted villi which might easily be mistaken for the chorionic villi of pregnancy. In somewhat more than 15 per cent of these patients the tubal pathology is believed to have been due to other pus-producing bacteria, notably streptococci. Tabulation of the gross changes encountered in these non-venereal infections reveals that, when salpingitis occurred, it was most often but a part of the pathologic picture rather than the chief lesion. Cases in which the tubes present the essential pathology seem unusual in such infections. The most notable exception to this is the fairly frequent occurrence of non-gonorrheal hydrosalpinx. Occasionally pyosalpinx complicates a puerperal abscess of the ovary. The diagnosis of salpingitis of a non-gonorrheal nature is usually possible even in the absence of growth in cultures. As just mentioned, the tubal changes may present but a minor part of the picture. The typical lesion consists in perisalpingitis with adhesions which vary in number and density. The adhesions are often delicate and few; this seems

particularly to characterize mild colon bacillus infections. On the other hand, virulent streptococci leave most dense adhesions without available lines of cleavage. Firmly bound, matted tissues, which resist all attempts at blunt dissection speak strongly for streptococcus or tuberculous infection. Even though there has been a primary gonorrheal salpingitis, adhesions which necessitate extensive cutting suggest that other infection has also been present. The tube walls may reveal little change and palpable induration is often wanting, while the fimbriated ends tend to remain patulous. The microscope most often fails to show extensive changes of the endosalpinx.

Pelvic Abscess. In a series of 716 cases of pelvic abscess reported by Wharton[1] from the Johns Hopkins Hospital, vaginal incision and drainage has been the only operative treatment employed in 67 per cent. The nature of this operative procedure and the propinquity of the pelvic abscess to the pelvic viscera make the occurrence of operative accidents an easy possibility. Because of these anatomic relationships, pelvic abscesses may also rupture spontaneously into the bladder, the rectum, vagina, the peritoneal cavity, or may burrow out into the retroperitoneal spaces and travel extensively. Operative or spontaneous rupture into the bladder or rectum leads to the formation of fistulas which greatly prolong the convalescence. The convalescence of patients with pelvic abscesses who have been treated by vaginal incision and drainage requires the greatest surveillance, as complications of a serious nature are common and require prompt treatment. The essential factors in the routine postoperative care are Fowler's position and prolonged drainage. The pelvic drain should not be removed for at least ten days. After it has been removed, the drainage tract should be dilated digitally every day or two to preserve its patency. Irrigation of the abscess tract is condemned.

The convalescence of patients with abscesses of puerperal or tuberculous origin is usually much more stormy, prolonged and febrile than that of any other type. In all cases of pelvic abscesses general hygienic measures should be employed to build up the strength of the patient. In all of the cases of pelvic abscess in this series without differentiation of the various types, the mortality following treatment by vaginal incision and drainage has been 5.1 per cent. In the gonorrheal type, the mortality has been 4.5 per cent; in the puerperal type, 13 per cent; in those which were tuberculous, about 25 per cent. It is rather difficult to obtain accurate statistics with regard to the mortality in cases of tuberculous pelvic abscess, because it is probable that in many cases in which laparotomy was not performed, the real nature of the infection was not recognized. The most frequent cause of death has been general peritonitis. The average length of convalescence of patients with pelvic abscess treated by vaginal incision and drainage has been from two to three weeks. Twenty-five per cent of the patients in this series have apparently been permanently cured by vaginal incision and drainage. These patients have been relieved of all symptoms and have been in

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[1] Archives of Surgery, 1921, **2**, 246.

perfect health for a period of from three to twenty-five years. Twenty-two per cent have been improved permanently, and in 56 per cent this treatment has resulted in ultimate failure in that these patients have not been permanently relieved of their symptoms. It is not possible to give an accurate prognosis in individual cases of pelvic abscess after this method of treatment. Although the prospect of obtaining a permanently good result is better in a patient in whom the immediate result has been good, the frequency of unexpected and acute exacerbations, puerperal infections, and persistent pain due to adhesions, make it impossible to make an accurate forecast in individual cases.

Tuberculous Salpingitis. An analytical review of 200 cases of tuberculosis of the tubes that were observed in the gynecological department of the Johns Hopkins Hospital has been presented by Greenberg[1] as a result of which he has been able to draw some rather interesting and instructive deductions. It was noted that tuberculosis of the tube occurred in nearly 1 per cent of all women admitted and was found one and a-half times as frequently among the colored women as among the whites. Out of every 13 abnormal tubes removed at operation, 1 was tuberculous and nearly three-fourths of the patients who had tuberculous salpingitis were between twenty and forty years of age, while 60 per cent of the married patients were sterile. A family history of tuberculosis was reported in 22.5 per cent while in an additional 2.5 per cent the consort had active pulmonary tuberculosis. The chief complaint of the patients was pain (74.5 per cent) usually situated in the lower abdomen. Not much information was obtained from the menstrual history although it was noted 62 per cent of the patients had dysmenorrhea and 41.5 per cent menorrhagia. Amenorrhea occurred in only 6.5 per cent of the patients. Nearly half of the patients had dysuria, nocturia and pollakiuria and more than half of the patients were constipated. Approximately one-fourth of the patients attributed the onset of their trouble to some uterine activity (menstruation, pregnancy, etc.). Half of the patients had lost weight during their illness but the physical examination presented no characteristic findings, except that one-fourth of the patients had pulmonary tuberculosis. Pre-operative elevation of temperature was recorded in 6.5 per cent. The blood usually showed either an absolute or a relative leukopenia and a reduced hemoglobin. The correct diagnosis before operation was made only in 13 per cent of the cases and in more than half of these the diagnosis was aided by the presence of ascites. In 53 per cent of the cases it was necessary to perform a radical operation, and complications during the operation occurred in 14.5 per cent of these patients. One hundred and four cases were drained and, of these, 17.3 per cent developed fecal fistulæ. In one-third of all these patients there was suppuration of the abdominal incision. In 99 per cent of the cases both tubes were involved, in 68 per cent the peritoneum was involved and in 3 per cent the appendix was tuberculous. The operative mortality in this series was 7.6 per cent but the prognosis is grave in the presence of tuberculosis elsewhere in

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[1] Bulletin of the Johns Hopkins Hospital, 1921, **32**, 52.

the body, where fever exists and where the peritoneum is involved. By means of follow-up letters 90 patients were traced, and of this number 78 were found to be living from two months to thirty years after the operations and nearly all of those who are alive are in good condition.

Drainage in Pelvic Surgery. The question of when to drain in the performance of pelvic operations is never ending, and from the extreme of universal drainage of some years ago, the pendulum has almost swung to the point where drainage had to be defended by the surgeon using it. The question can only be answered by long and varied experience under all sorts of conditions and there is probably no gynecologist in this country whose opinion along this line should bear more weight than Kelly's.[1] He feels sure that from time to time the judicious use of a drain over a short period of time, from thirty-six hours to several days, does one of three things: It is an unspeakable comfort to the surgeon to be sure that there is no collection of fluid about the field of operation. It relieves the patient of a vast amount of discomfort in her early convalescence, converting a stormy, febrile recovery into a smooth, peaceful one. It carries off the serum and blood, and, it may be, lingering infections which occasionally give rise to a general peritonitis. Kelly would drain in every case where infectious material has been widespread and there remain some lingering suspicious areas. He includes here cases in which there has been soiling by bowel content. He would drain in all ragged cases such as those in which pelvic adhesions had been so extensive and firm about the floor and walls that the occurrence of considerable serosanguinous weeping is a moral certainty. Without exception, he drains after removing a cancerous uterus. He uses a small, special drain in most cases of myomectomy, where sometimes weeping and bleeding occur unaccountably. When in serious doubt, Kelly says drain! Some surgeons would undoubtedly reverse this dogma. If the trouble in the pelvis is very severe, then a good drain of washed iodoform gauze in protective rubber tissue ought to be laid through the vaginal vault, to cover the pelvic floor loosely. It should never be packed in tightly and never, under any circumstances should the drain be allowed to extend up or down between loops of bowel. A form of drain which he has found most useful in his work, and which he calls a provisional or tell-tale drain, is a small drain about the size of a cigarette or a little larger. It is laid through the abdominal wall at, or near, the lower angle of the median incision, above the symphysis, reaching well within, but no attempt is made to come in contact with the field of operation which lies, it may be, well below the pelvis. He uses such a drain in myomectomy as well as where serious oozing is to be expected, but never where there is reason to expect immediate infection. Its sole function is to let out all the excess of serum and blood welling up from the pelvis and seeking this direction of least resistance. It is temporary in character, being removed in from twenty-four to thirty-six hours, as soon as the outward flow abates, as shown by the dressings remaining dry.

[1] New York Medical Journal, 1921, **114**, 390.

Gynecologic Significance of Appendicitis in Early Life. It seems to be well established that the appendix may undergo considerable grades of inflammation and yet eventually be restored to a condition of approximate normality. It is entirely probable that during the inflammatory periods of a chronic appendicitis, a serous or serofibrinous exudate is produced which finds its way by gravity into the true pelvis since one often encounters such an exudate in apparently uncomplicated pelves and wonders whence it came. Therefore, Graves[1] believes that it is quite reasonable to suppose that, although this exudate is usually absorbed by the peritoneum, under certain conditions it may be sufficient, either through bacterial or chemical influence to destroy the superficial epithelium of the pelvic peritoneum and to stimulate the subserous connective tissue into the formation of organized plastic adhesions; or it may itself become organized and form the basis of adhesions. In this way may be explained theoretically the cases not infrequently encountered in which, without sign or history of gonorrhea or puerperal sepsis, adhesions are found in the posterior cul-de-sac, or implicating the surfaces of the adnexa while the appendix shows only mild evidence of the disease, or perhaps none at all, to gross appearance. If besides the pelvic adhesions there is added a well-defined chronic appendicitis, or the scar of an appendix operation performed in youth, Graves believes his explanation is still more plausible; certainly more so than the attempt to ascribe the condition to an entirely improbable gonorrheal infection. For this reason appendicitis in childhood or young girlhood is an affection which must be regarded not simply with reference to the diseased organ itself but to the serious harm which it may exert on the pelvic organs, if left to work out its own destiny in the state of chronic inflammation. Early operation is therefore indicated in children when there is a suspicious evidence of appendicular infection. In the acute stage the appendix should be removed immediately to forestall, if possible, a secondary involvement of the adnexa. If pus is present, every effort should be made to drain the pelvis, it being feasible in certain cases to drain the pouch of Douglas through the vagina. Excepting in cases of localized abscess it is advisable to make a median line incision in order that the pelvic organs may be inspected, and that any abnormalities of position or plastic adherence may be remedied by a proper surgical procedure.

Varicose Veins of the Female Pelvis. Perhaps no other subject in the large field of gynecology has been treated so negligently as the one on varicose veins of the female pelvis. This subject has, however, received considerable attention at the hands of Emge,[2] who states that the symptomatology centers around one point, and that is the pain complained of and which must be carefully analyzed. One usually hears that beginning with a definite time there have appeared either bilateral or unilateral, usually, left-sided pains of a dull, deep, aching character felt low down in the abdomen which grow worse on long standing and are relieved quickly when the patient assumes the recumbent position. This one complaint is just as typical for women as it is for men who

[1] Archives of Surgery, 1921, **2**, 315.
[2] Surgery, Gynecology and Obstetrics, 1921, **32**, 133.

suffer from varicocele and to which the condition in the female has been likened. If sufficient attention is paid to this point, the history becomes suggestive enough to make the examiner look for these veins. All of the other symptoms are obscure and they hold good for almost any pelvic disturbance. There is commonly a sense of heaviness in the pelvis and the patient often suffers from constipation. As the patient is usually examined in the recumbent position, her veins are well drained, and therefore, they are not palpable. One would never fail to examine a man standing up if he would complain of anything pointing to trouble around the genital organs, but custom has made the recumbent examination in women a standard. If one will take the trouble to examine the patient by recto-vaginal touch in the recumbent position and then have the patient drop her legs and raise her upper body, Emge believes that it is often as easy to feel these veins in the female as in the male, for the veins will fill quickly and bring out the dilatation and tortuosity in the shape of an easily compressible and doughy tumor that is much less tender than either an inflamed or an ectopic tube. The tumor will disappear again when the patient resumes the recument position. Furthermore, Emge believes that ovarian varicosities are frequently overlooked during exploratory operations for pelvic disturbances, because the habit of having the patient put into the Trendelenburg position before the incision is made is quite common, thus putting the veins in the most favorable position for good drainage. Considering the treatment of this condition, if the ovarian or uterine venous units become distended as a result of constipation, the first principle naturally must be to regulate the bowel and, if visceral ptosis is present, a proper abdominal support must be added. During the period of any conservative treatment it is essential that the patient keep off her feet as much as possible so that the veins of the broad ligament may be in the most favorable position for free flow and all sexual excitement must be prohibited. Hot douches should not be given as they increase congestion, but slow lukewarm douches with 2 or 3 per cent of menthol and 5 per cent of alum will produce a pleasant cooling effect. When the veins have distended to such a degree that one must suppose that they cannot return to normal, operative procedures must be considered. Emge does not advise resection of the distended veins nor resection of cystic ovaries as the number of symptomatic reliefs that he has obtained is sufficiently large to indicate that suspending operations, if carried out properly and in conjunction with utero-sacral shortening, will give the desired result in the cure of varicose veins of the broad ligaments and of the ovarian veins in particular.

Primary Pelvic Lymphadenitis. Although no little study has been given to the lymphatic glands of the pelvis from both the anatomic and clinical standpoint, such investigations have been practically limited to the consideration of these glands in malignant disease of the uterus or other pelvic organs. The possibility of non-malignant disease of these glands, as well as that of primary malignant lymphatic disease seems to have been overlooked. The occurrence of 3 cases of enlargement of the pelvic glands giving rise to striking clinical manifestations

during a two months' service has led Williams[1] to believe that pelvic masses consisting of such glandular enlargements must be of not infrequent occurrence although seldom recognized. The term primary disease of the pelvic lymphatic glands, is perhaps somewhat inaccurate inasmuch as with the sole exception of lymphosarcoma or Hodgkin's disease, involvement of any part of the lymphatic tract must be secondary to a process in some other organ or tissue. He has selected the title, however, to differentiate those cases in which the enlargement of the glands in itself gives rise to important clinical manifestations, from those in which the enlargement of the glands is solely a measure of the extent of a malignant process in another organ. An analysis of the cases which Williams has observed shows that a mass in the pelvis close to the pelvic brim and definitely not connected with the uterus or its appendages was present in all 3 cases. Pain was always present and in 2 cases it was localized in the right iliac fossa and in 1 it was along the course of the ureter and in the kidney region and was due to occlusion of the ureter by pressure of the glandular mass from without. Psoas spasm was present in 2 of the 3 cases and must be regarded as quite an important symptom. Of course, an *x*-ray of the spine is necessary to rule out the mass and contracture due to psoas abscess from spinal caries. The leukocyte count in these cases, even the one with abscess, ranged between 9000 and 11,600. Further observations may or may not reveal higher white counts in more virulent infections. The white count obviously must be influenced in great part by the particular organism concerned as well as the resistance of the patient.

Postperitoneal Tumors. In reporting a case of postperitoneal cystoma, Graves[2] discusses the histogenesis of postperitoneal tumors in general. They appear in a great variety of forms including fibroma, fibrosarcoma, lipoma, simple serous cystoma, multilocular serous cystadenoma, teratoma, dermoid cystoma, etc. One may readily imagine that such tumors as the fibromata and lipomata have their origin in the subperitoneal cellular tissue in a manner entirely analogous to that which they exhibit in any other part of the body. The unusually large size that they may attain postperitoneally is undoubtedly due to the slight tissue resistance that they encounter during their growth. One may also imagine that some of the simple serous cysts may arise from isolated rests of the Wolffian ducts.

The histogenesis of certain of these growths is, however, not so easily explained. Especially is this true of the dermoids and teratomata. These tumors, whether they arise in the ovaries or postperitoneally, are unquestionably ovigenous. Their development in the postperitoneal cellular tissue has usually been attributed to misplaced blastomeres that after the original segmentation, have wandered away from their normal place of assembly in the genital gland and have become isolated at some point in the postperitoneal space. The acceptance of this explanation implies a belief in the germplasm theory of Weissman, which asserts that the germ cells (ova and

[1] Boston Medical and Surgical Journal, 1921, **184**, 194.
[2] Surgical Clinics of North America, June, 1921, p. 607.

spermatozoa) are entirely independent in their relation to the body or somatic cells, both in origin and growth. Recent studies in the embryologic development of the germinal epithelium covering the ovary have done much to disprove this theory. Thus it has been shown that the genital gland originally develops from the germinal epithelium, which itself is a local modification of the peritoneum. The growth in size of the genital gland is due to an invasion downward of the germinal epithelium, and it has been shown that all the cellular elements of the ovary, with the exception of a fine connective tissue framework, are derived from the down-growing germinal epithelium. These cellular structures include the stroma, interstitial cells, the remains of the rete ovarii, and cords of Pflueger, the granulosa layer of the Graafian follicles and finally the ova themselves. It may be seen, therefore, that the ovarian dermoids and teratomata being ovigenous, are derived in the last analysis from the germinal epithelium. It has also been conclusively proved that the serous cystadenomata are derived directly from the germinal epithelial layer that invests the ovary. Bearing these facts in mind, Graves argues that if the embryonic peritoneum has the power of a local differentiation into a germinal epithelium, which in turn may produce germ cells, it is entirely conceivable that this power of differentiation may abnormally appear in parts of the peritoneum other than that portion which is eventually destined to become a genital gland. In this way cells may be created in different areas of the subperitoneal space exactly similar to those in the ovary which have the power of becoming dermoids or teratomata.

THE OVARIES.

Perforating Hemorrhagic Cysts of the Ovary. One of the outstanding pieces of work which has been contributed to the realm of gynecology during the past year has been the investigation conducted by Sampson[1] upon the subject of perforating hemorrhagic, sometimes called "chocolate," cysts of the ovary in which he has brought to our attention the relation of these apparently unimportant cysts to pelvic adenomas of endometrial type, commonly known as adenomyoma of the uterus, recto-vaginal septum, sigmoid, etc. These cysts occur most frequently in women between thirty years of age and the menopause and they are quite common, probably occurring in nearly 10 per cent of the women of these age limits who require abdominal operations for the relief of pelvic disease. The cysts are usually small, between 2 and 4 cm. in diameter, occasionally less than 2 and also occasionally larger than 4 cm. and are quite frequently bilateral. At operation, the cyst or ovary is found to be adherent, and, in freeing it, the "chocolate" contents escape because a previous perforation, which had been sealed by whatever structure the ovary had become adherent to, is reopened or the cyst is torn. Adhesions, due to the irritating action of the material which had previously escaped from the ovary, are always present, and these vary greatly in

[1] Archives of Surgery, 1921, **3**, 245.

location, density and extent. They may be found in any of the natural pockets or folds of the pelvis where such material would be likely to lodge, and especially in the cul-de-sac. When slight, they simulate the adhesions resulting from pelvic peritonitis of tubal origin. On the other hand, the adhesions in the cul-de-sac may be accompanied by such a marked reaction as to resemble malignancy. The histologic findings in these cysts vary in different specimens and in different portions of the same cyst. There may be several varieties of these cysts but Sampson is inclined to believe that most of the apparently different kinds represent various stages in the development and retrogression of one type of cyst and the various phases in its "menstrual" cycle. The initial perforation may have been the rupture of an "endometrial" Graafian follicle or atretic follicle hematoma; or, following ovulation, an abnormal corpus luteum may have developed due to the invasion of "endometrial tissue" present at the site of rupture. One group of these perforating hemorrhagic cysts show these conditions: A portion of the hematoma, usually the deeper, is lined by "a luteal" membrane, the exact origin of which in some specimens is difficult to state. The rest of the cyst, usually toward the perforation, is apparently being relined by the invasion of the epithelium, through the perforation, from epithelium situated in the periphery of the ovary at the site of rupture. This epithelial relining or regeneration is of endometrial type, both in structure and in function. With the advance of the epithelial invasion, the "luteal" membrane retrogresses, and eventually the entire cyst may be relined by this epithelial tissue. This group represents either the development of an "endometrial" cyst from the invasion of a follicular hematoma by misplaced "endometrial" epithelium or else it represents the regeneration of an "endometrial" cyst after a hemorrhage.

Another group apparently represents either an earlier or a later stage of the former. The cysts in this group are entirely lined with epithelium, low, cuboidal or columnar; all three types of epithelium are often found present in the same cyst. Usually there is a vascular cellular stroma not unlike that of the endometrium, between the epithelium and the ovarian tissue, often with evidence of old and recent hemorrhage. This stroma varies greatly in thickness and in some instances may be very thin or lacking. Structures, like uterine glands, may be present in this stroma, and these are usually most numerous near the site of the perforation. The entire cyst is like the epithelial portion of the cysts described in the first group, and all gradations between the two groups may be found. The exact counterpart of the epithelial lining of these ovarian hematomas may be found in the uterine hematomas often occurring in "adenomyoma" of the uterus and apparently due to the retention of menstrual blood. Tissue of endometrial type is also present in pockets in the periphery of the ovary about the perforation, and the tissue in these pockets may resemble normal endometrium more closely than that lining the hematoma in the same ovary. The histologic study of these hematomas shows that periodic hemorrhage similar to that of menstruation occurs and Sampson has come to the conclusion that these ovarian hematomas are of endometrial type just as are the uterine hematomas found in "adenomyoma" of the uterus.

The adhesions form equally as interesting a pathologic study as the cysts themselves because adenomyoma of endometrial type is present in the tissues involved by the adhesions in a large percentage of the cases. Some time, or possibly many times, in the life of these hematomas, material, including epithelial tissue and blood, may escape into the peritoneal cavity from the hemorrhagic cyst or from the "endometrial" pockets in the ovary about the site of perforation and, lodging in the natural pockets and peritoneal folds of the pelvis, they may cause adhesions. Adenoma of endometrial type often develops between the adherent folds of peritoneum thus resulting. These adenomas may be small and quiescent or they may be invasive. If invasive, they may cause adenomyoma of the uterus by invasion of the uterine wall from without or adenomyoma of the utero-sacral ligament, round ligament, recto-vaginal septum, rectum, sigmoid, etc., namely, whatever structure is invaded by the adenoma arising from the infective contents of the cyst or ovary lodging on its surface. The question naturally arises. In what way do the contents of the cyst or ovary cause the development of these adenomas? Is it due to some specific irritant present in the cyst contents which stimulates the peritoneal endothelium, thus causing a metaplasia and the development of endometrial tissue typical both in structure and function? Some may assert that dormant endometrial epithelium may be present in the tissues soiled by the contents of the cyst and this is stimulated to further growth. Sampson thinks that the condition found in many of these specimens is analogous to the implantation of ovarian papilloma or cancer on the peritoneal surface of the pelvis from the rupture of an ovarian tumor containing these growths.

Sampson summarizes the following data as evidence that perforating hemorrhagic cysts of the ovary are hematomas of endometrial type.

1. These hematomas, as the uterine mucosa, manifest their activity during the menstrual life of the patient.

2. Histologically, the epithelial lining of the ovarian hematomas is similar to that of the uterine hematomas, due to the retention of "menstrual" blood, often present in adenomyoma of the uterus.

3. Periodic hemorrhages occur in the ovarian hematomas which are similar in gross and histologic appearance to that of menstruating endometrium.

4. The "chocolate" contents of the ovarian hematomas resemble old menstrual blood.

5. In two patients operated on at the same time of the menstrual period, one the day that menstruation was due, and the other the last day of menstruation, the histologic changes in the ovarian endometrial tissue corresponded to the phase of the menstrual cycle indicated by the menstrual history of the patient.

6. The fact that material escaping from ovarian hematomas may give rise to the development of adenoma of endometrial type in the tissues thus soiled is further proof that these hematomas contain endometrial tissue.

He does not state that these ovarian hematomas of endometrial type are the only cause of ectopic pelvic adenomas but nevertheless perfora-

ting hemorrhagic cysts of the ovary with their secondary peritoneal implantations are a pathologic entity as definite as that of ovarian papilloma and cancer and should be diagnosed before operation in a large percentage of the cases.

In regard to the treatment of this condition, Sampson states that he has never resorted to the extremely radical operations, as in cancer of the uterine cervix, and even in these operations it may be impossible to remove all of the adenomatous growth. In the radical operations which he has employed, he has removed the entire uterus with both ovaries, and in freeing the uterus from the rectum he has purposely kept close to the uterus, undoubtedly sometimes leaving adenoma in the rectal wall. His present plan, however, is to employ ovarian conservatism (excising the portion of the ovary or ovaries involved) or removing only the apparently diseased ovary in patients who desire to have the ovarian function maintained but only when the invasion of the pelvic tissues by the adenoma is slight. In all other cases, either when ovarian conservation is not strongly desired or when the pelvic growth is apparently actually invasive, he believes that all ovarian tissues should be removed and as much of the pelvic growth as possible.

Papillary Cystadenoma. In a review of 5000 consecutive pathologic sections of the Pathological Department of the New York Post Graduate Medical School and Hospital conducted by Erdmann and Spaulding[1] cystic disease of the ovary constituted 200, or 4 per cent, and of the 200, 36, or 18 per cent were papillary. Nothing in ovarian literature is more confusing than the histogenesis of cysts, particularly the papillary. Every embryologic and histologic structure has contributed a theory of origin, and considering the number of structures from which the ovarian tumors might arise, and the confusing multiplicity of views, no definite conclusion as to the exact histogenesis has yet been reached. Their review has impressed them with two facts: The very gradual transition, with no sharp line of distinction or classification from the benign to the premalignant and to the typically carcinomatous picture; and that a simple, apparently benign, papillary area may exist in the same section with a complex or malignant field, from which clinically one can only conclude that there is no clinical method whereby the degree of malignancy can be determined except by the microscope. In the 36 cases studied in this series, 33 per cent were benign, 16.6 per cent were premalignant, and 50 per cent malignant; 22.2 per cent were bilateral, and 13.8 per cent multilocular. Therefore out of 200 cases of all types of ovarian tumors, 12 per cent were malignant or premalignant papillomata.

There is no specific ovarian symptomatology. The subjective symptoms are in every case referable to other organs and the objective symptoms are vague, uncertain and often absent. The symptoms are dependent largely on the size of the tumor and whether or not rupture or pedicular torsion has occurred. The diagnosis of papillary cystadenomata is difficult in the unruptured state, is at times very uncertain

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[1] Surgery, Gynecology and Obstetrics, 1921, **33**, 362.

after rupture, and is only positive in the rare instances when the papillary masses are palpable or visible in the vagina. The small adherent mono-cystic tumors are more liable to be papillary than the large movable and polycystic masses, while bilateral masses are open to more suspicion. Hydroperitoneum without a sufficient explanation in the liver, heart, peritoneum, and kidneys is most suspicious of the existence of the papillary peritonitis even though bimanual examination be negative.

The prognosis is variable. However, one must bear in mind that the papilla *per se* implanted upon or invading the surrounding tissues or organs, is never in the true clinical acceptance of the word, benign. On the other hand it rarely shows the rapid progress of neoplasms associated with other glandular or structural tissues. As shown by the critical examination of a series of microscopic sections, many typical papillary sections have a carcinomatous process developing at the same time and microscopically 66.6 per cent of the cases in this series were malignant or potentially so. Many of the patients are prone to live a variable number of years after operation and have been operated upon from two to five times in a period of ten years.

Considering the treatment, in the unruptured state the cyst must be removed intact regardless of the length of the incision required for its delivery *in toto*, as there is no way of distinguishing the benign adenoma from the adenocarcinoma except by microscopic section after its removal. The cyst wall is the thin dividing edge of malignancy, and of all neoplastic growths we are the most favored in the ovarian variety of tumors by this natural wall of separation between health and disease. The adhesions are separated and the cyst is liberated with all gentleness. Careless manipulation resulting in rupture within the peritoneum cannot be too highly con-demned. Regardless of the size of the tumor it should not be reduced by tapping, bearing in mind that even the large glandular pseudomucin-ous tumors are often studded with papillary growths. The fluid contents of the cysts rich in desquamated epithelial elements, must, under no circumstances contaminate the peritoneum. The vaginal route should never be attempted in the removal of an ovarian tumor. In the rup-tured state, paracentesis alone is of little or no avail in influencing the course of the disease and has long since been discarded as a therapeutic measure. Upon laparatomy the fluid is evacuated and the peritoneum inspected; if the growth is localized, the indications are simple, but if the disease is extensive a panhysterectomy should be performed, as carefully as possible approximating the edges of the broad ligaments and inverting the ovarian pedicles. A careful toilet of the peritoneum should be made, sacrificing infiltrated portions of the omentum or parietal peri-toneum. Drainage is rarely indicated. With recurrence of ascites and the associated symptoms, it may be necessary to remove further portions of the growth by reoperation. In unilateral cases, one ovary and tube should be retained in the childbearing age unless the disease is dissemin-ated or unless the diseased ovary shows gross evidence of malignancy. Sterility is preferable to an incomplete operation when the growth is at all suspicious. If, however, the other ovary is left *in situ* periodical

examinations should be made. Inasmuch as the normal ovarian tissue is particularly sensitive to radiant influence, and moreover, as ovarian papillomata have a relatively low metastasizing power, cases in which the growth has been incompletely excised should be given the benefit of radium. In every case which has undergone cancerous degeneration, *x*-ray and radium treatment should be given in addition to the operative procedure. An exploratory laparotomy should be done in every advanced case of suspected ovarian carcinoma (unless, of course, the general condition of the patient contraindicates) to establish the diagnosis, for even though there is much ascitic fluid in the abdomen and palpable nodular masses, no carcinoma may be present, and moreover, one or both ovaries may be still unruptured.

Enormous Ovarian Cyst. A case of an ovarian cyst which weighed more than the patient who carried it has been reported by Harley[1] and reminds us of the type of cases that were quite prevalent before the day when Ephraim McDowell showed the way to the medical profession by performing his classic ovariotomy. In the case reported by Harley, the patient had noticed an enlarged abdomen over a period of fifteen years and at the time of operation she weighed 246 pounds, while immediately after operation she only weighed 82 pounds. Thus the tumor and its contents weighed 164 pounds or twice as much as the patient herself. It is unfortunate that the patient did not survive the operation, although it could hardly be expected that she would have much resistance when in such a physical condition.

Tumors of the Ovary in Children. In reporting a case of a large ovarian cyst in an infant seven months of age, Downes[2] warns that any tumor of the ovary, cystic or solid, should be removed as soon as possible after its discovery as there is nothing in its early clinical history to indicate whether the condition is benign or malignant. As naturally expected, a swelling in the lower abdomen is, as a rule, the first sign to call attention to the fact that the infant is suffering from an ovarian tumor. This may be observed at birth or soon thereafter. However, in many of the recorded cases, acute abdominal pain due to twisting of the pedicle was the first symptom noted. The history of a number of cases states that a previously healthy child begins to run down and show constitutional symptoms before the presence of a growth is made out. This generally suggests malignancy. Other symptoms are those due to the presence of the mass in the abdomen and vary according to the size and consistency of the tumor. Owing to the fact that the uterus and its appendages are practically abdominal organs in early infancy, pressure symptoms on the rectum and bladder are seldom encountered. In the case of solid growths, especially if accompanied by adhesions, there may be disturbance of the bowel, pressure on the ureters and bladder, and ascites. The growth may reach such proportions as to interfere mechanically with respiration and the general comfort of the patient. On the other hand, it is surprising how little the simple cystic tumors may interfere with nutrition. The fact that the infant takes its feedings well and

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[1] Indian Medical Gazette, 1921, **56**, 18.
[2] Journal of the American Medical Association, 1921, **76**, 443.

seems to thrive in spite of the presence of a large cystic tumor greatly favors the absence of malignancy. In older children, the early appearance of menstruation or an irregularity in it has been noted.

The diagnosis of ovarian tumors in infants offers several difficulties. In the first place, the condition is so unusual that the examiner may not give due consideration to the possibility of the existence of such a disease. These growths are abdominal rather than pelvic, and are usually attached by a long pedicle. For this reason they are easily mistaken for kidney tumors, mesenteric cysts, etc. If, however, the mass occupies the midhypogastric region, and rectal examination suggests the presence of a pedicle giving a cord-like feel to the finger, the diagnosis may be easily made. In the case of large cystic tumors occupying almost the entire abdominal cavity, a general consideration of the patient will be of great value. The question of an anteoperative diagnosis is of little consequence as compared to the importance of early removal, and for this reason valuable time should not be wasted before resorting to an exploratory incision.

Fibroids of the Ovary. Ovarian fibromata comprise approximately 2 per cent of all ovarian tumors and may occur from the time of puberty to an advanced age. The majority occur in single women about the time of the menopause. The size and weight of these tumors vary extremely and the etiology has always been obscure. In reporting a case of this comparatively rare condition, Clark and Gabe[1] state that in the majority of reported cases the patients have complained of a swelling of the abdomen, pain of varying degree, often none at all, and not infrequently of feeling a hard mass through the abdominal walls. Other symptoms, such as frequency of urination, constipation, etc., are due to varying mechanical factors. Objectively, the tumor is usually palpated without difficulty. Its consistency, mobility and unilateral occurrence are significant. One feature, however, is of marked diagnostic importance when present, namely, ascites. The weight attached to this finding has been especially emphasized by English writers on the subject. It may be recalled that fibroma elsewhere, and especially in the uterus is rarely associated with ascites. The presence of ascites with intra-abdominal carcinomatosis, located either primarily or secondarily in the ovary as a tumor mass, is common, but is associated with many other signs and symptoms not found in fibroma of the ovary. In other benign tumors of the ovary, ascites is usually lacking. It therefore seems of considerable diagnostic importance to find ascites together with a unilateral adnexal tumor in a case lacking cachexia, great loss of weight, or symptoms pointing to a focus of malignancy elsewhere in the body, as in the breast or stomach. In the absence of ascites, differential diagnosis from other adnexal tumors offers considerable difficulty. The tendency of ovarian fibromata to be unilateral, movable and hard, should be borne in mind. In the presence of ascites, when nephritis, cardiac decompensation, portal obstruction, abdominal carcinoma, tuberculous peritonitis and the anemias can be ruled out, the occurrence

[1] American Journal of Obstetrics and Gynecology, 1921, **1,** 603.

of such findings should make one very suspicious of ovarian fibroma. The treatment, without exception, is operation. The prognosis, as indicated from case reports, is excellent. The pathology of ovarian fibroma has been carefully studied by several investigators, showing that these tumors vary in size. Their consistency, likewise, is extremely variable, some, composed of a loosely woven network of connective tissue, being soft, while others require the use of a bone saw for their section. In a similar way, their shape, appearance on cross section, color and general outline cover a wide range of possibilities. They show many forms of degeneration and it is on account of these, as well as the possibility of a twisted pedicle, that their removal should be urged. The court of final judgment is the microscopic appearance of the tumor.

Clinical Experience with Corpus Luteum Extract. The distressing symptoms of the menopause may be relieved quite frequently by the administration of corpus luteum extract, according to Leighton[1] since luteum extract supplies that element so necessary to the woman during her normal menstrual life. This therapy exerts its greatest benefit in the treatment of those women who have begun to exhibit the early manifestations of the climacteric. To avoid the unsatisfactory results which have been reported by some gynecologists, it is necessary that luteum extract be administered early and continuously once the diagnosis is made. Procrastination on either the part of the patient or the physician often means ill-success. When menstrual irregularity makes itself known and the hot flushes, mental confusion, tremor and hyperthyroideal symptoms are first evident, then is the proper time for organotherapy, not waiting until the height of the disorder has been reached or the woman has suffered for months or years with a "chronic" menopause. Early control is necessary, and once obtained, is easily maintained. In over half of the 300 or more women to whom Leighton has given luteum extract, the indication for its use was solely for the menopausal syndrome. Of this number there were not over a dozen who could not report exceptional benefit, even to absolute relief.

To those women who, during the menstrual life, complain of so-called "sick headaches" of the frontal and temporal type, with nausea and vomiting, which occur with peculiar periodicity, at or about the time of menstruation, ovarian organotherapy offers much relief. In chlorosis, as an adjunct to hematinics, luteum is also indicated. The functional amenorrhea of women in early adolescence or midmenstrual life, responds in a miraculous manner. In the use of thyroid as a "reduction cure," the giving of luteum at the same time seems to obviate the occurrence of profuse sweating spells, muscular weakness, tachycardia, nausea and other vasomotor symptoms, occasionally following the ingestion of thyroid extract. Larger doses of thyroid are tolerated if given in conjunction with luteum. While Leighton has not had 100 per cent of success, it has been his fortunate experience to observe a relief and cessation of many disorders referable to deficient ovarian secretion, where proper diagnosis is followed by the continuous, thorough and regular

[1] American Journal of Obstetrics and Gynecology, 1921, **1**, 613.

use of luteum extract. It is important above all, that the physician should prescribe and the patient obtain a product from recent fresh material and care must be taken to see that the dispensing chemist has such on hand. The indiscriminate buying of luteum extract is one thing which Leighton is careful to prevent by directing his patients to a shop where he knows that fresh material may be had. Each prescription calling for such bears on the direction label, "these must be taken for ten or twelve weeks" and special emphasis is laid upon this point. He explains every time, at the commencement of treatment, that it is cumulative in action, is non-toxic when fresh, and that one must be conscientious in taking the medicine, as results are obtained slowly and relief is not immediate.

THE VAGINA AND VULVA.

Construction of Artificial Vagina. The technic which Graves[1] employs in the construction of an artificial vagina begins with a transverse incision, about two inches in length, which is made across the space usually occupied by the introitus. With blunt dissection, a plane of cleavage is sought beginning just above the commissure of the levator ani muscles. It will be found that the tissues may be separated with comparative ease, but some bleeding is encountered so that it is necessary to proceed cautiously with the dissection. In this way an opening is made which corresponds in its proportions to a normal vagina. It is important not to enter the abdominal cavity. Several catgut sutures with long ends are placed in the vault of the new opening and the ends tucked into the pouch for later use, as will be described.

The second part of the operation is to line the opening thus formed with skin turned in from the surrounding parts which may be best accomplished in the following manner: The labia minora are first partially amputated, the incisions being near the clitoris and continued downward toward the artificial opening, but leaving sufficient pedicle to allow competent circulation. The skin layers of the partially amputated labia are then separated so that they appear as paddle-shaped flaps. Two similar flaps are then dissected from the thighs. A third and if need be a fourth may be taken from the buttocks. In outlining the skin flaps it is important to mark the pedicles of the paddle-shaped areas in a *curved* direction. By observing this rule the flaps may be turned face outward without causing disagreeable folds at their attachments near the artificial opening.

The skin wounds made by the removal of the flaps having been sewed, a glass form, such as is used for maintaining a dilatation of the vagina, is placed at the artificial opening but pointing *outward*, the five or six skin flaps are sewed together over the glass form, the flaps being turned so that the skin surface faces externally. Great care should be taken to secure accurate coaptation of the skin edges and to fit the cap of skin smoothly over the glass form. When the sewing of the skin flaps has

[1] Surgical Clinics of North America, June, 1921, p. 611.

been completed, the ends of the sutures that had been attached to the vault of the artificial pouch are now brought out, threaded into needles and passed through the dome of the cap made up of skin flaps. By carefully inverting the cap, the artificial pouch becomes lined with a layer of skin which may be fastened snugly in place by tying the sutures that had been placed in the vault. The final step in the operation is to close with catgut sutures the remaining openings in the skin flaps at the introitus.

Vaginal Cysts. The clinical importance of vaginal cysts is not extensive, neither are they of extreme rarity; their interest lies chiefly in their origin, for which there are several possibilities. In presenting this subject Strong[1] reminds us that traumatism or operative enclosure may result in a cyst without characteristic features. More interesting are heterotopic vestibular or cervical glands which may give rise to cysts of the lower or upper vagina. Apart from such misplacement of the glands, it must be noted that the squamosa of the vagina may, through faulty development, be replaced by columnar epithelium and this may give rise to glandular structures which may become cystic. Vaginal cysts from such an origin are likely to be small, multiple, with low columnar epithelium which may be in true papillæ. The most interesting form of cyst is that derived from the Wolffian or Gaertner's duct, and this type may be of considerable size. It is interesting in point of size, in point of complexity of form, and in its predilection site, but apart from these considerations it must be admitted that origin from the Wolffian duct is largely inferential and that there is no determining characteristic. There are three sites of predilection of Wolffian cysts, namely, the epoöphoron, the ampulla and the lowest portions of the vagina inclusive of hymen. Abnormalities in form and course of the ducts occur. The epithelium is so variable and individual that one can hardly speak of true abnormalities, and squamous epithelium has been found in adults. Cysts are the commonest variation from the persisting duct and occur in various sites. Finally, adenocarcinoma and adenomyoma may be formed from rests.

Operation for Recto-vaginal Fistula. Although not claiming originality for the procedure, Hubbard[2] describes an operation for the cure of recto-vaginal fistula which seems to have considerable value in selected cases. It should be remembered that the condition causing a recto-vaginal fistula almost necessarily leaves a woman with a badly torn perineum, therefore this operation is planned not only to cure the fistula but also to repair the perineum. A curving incision is made at the line of junction of the mucous membrane of the vagina and skin and a flap of mucous membrane is turned up from the floor of the vagina until the fistulous tract made evident by a probe passed through it is reached. The tract is then dissected out intact, separated from the vaginal opening, but not from the rectal opening. A hemostatic forceps is then passed through the fistula from the rectum, fastened to the vaginal end, then pulled back through the rectum, turning the fistula inside out.

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[1] American Journal of Obstetrics and Gynecology, 1921, **1**, 357.
[2] Surgical Clinics of North America, June, 1921, p. 867.

Should the fistulous tract be too small to admit even a mosquito hemo-
static forceps it might be possible to accomplish the inversion by passing
a suture from the vaginal end of the tract through the fistula and out of
the rectum.   A pull on this would invert the tract unless its lumen were
too small to accommodate the thickness of even its own wall.   By put-
ting some tension on the fistulous tract thus turned inside out, the sides
of the fistula where it passes through the rectal wall, are brought together.
The opening in the rectum is then closed on the perineal side by catgut
sutures which may be placed so that the knot is in the rectum or not.
The excess of tissue containing the fistula is cut away, the opening in the
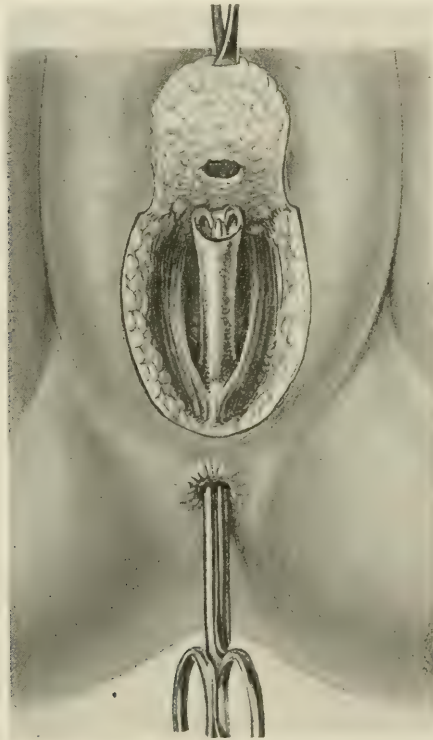
FIG. 3.—The beginning of the inversion of the fistulous tract.   (Hubbard in "Surgi-
cal Clinics of North America.")

vaginal mucous membrane is closed and the perineum is repaired by
pulling the muscles on either side of the denuded area together by buried
catgut sutures.   The operation is naturally most easily done when
the fistula is situated low down, but is applicable to one higher up, the
limit being determined only by the accessibility.   It has the distinct
advantage of entire removal of the fistulous tract and separation of the
suture line in the rectum from that in the vagina by a considerable
distance, by the aid of the plastic, which places the thick bellies of the
perineal muscles between the two suture lines, thus materially decreasing
the chance of recurrence.

Gehrung Pessary for Cystocele. The advantages and method of use of the Gehrung pessary in the relief of cystocele has been emphasized by Ill[1] who reminds us that the pessary consists of the Hodge instrument bent on itself so as to form a double horseshoe, one lever being a little shorter than the other. Its object is to hold up the anterior wall of the vagina and, with it, the bladder. The position of the pessary is such that the smaller horseshoe or lever will be placed anterior and below the cervix, while the larger one will be just above the neck of the bladder. The junction of the two horseshoes will remain in the lateral fornices. To fit well the pessary should be freely movable and not felt by the patient on walking or sitting down. In fact she should not be conscious of wearing the instrument except that she is comfortable, has lost the dragging sensation and the irritable bladder. The introduction of the instrument is rather difficult to describe. The pessary is held between the thumb and the fingers of the right hand by the rounded end of the horseshoe, the smaller one being forward. The connection between the horseshoe to the patient's left is introduced first and then with a rotary motion of 180 degrees the whole pessary is slipped into the vagina where another rotation of 180 degrees will put it into place. Care should be taken that neither horseshoe slips behind the cervix, in which case it will have to be removed and reintroduced, for the cervix will form a bar over which the pessary cannot be slipped. It goes without saying that experience and trial can only determine the proper size of the instrument to be used for each case. It is better to start with a small sized pessary and allow the patient to walk about the office as a test than to use a large instrument which may cause pain and injury. Ill states that those who will take the trouble and patience to master it will find great satisfaction for themselves and secure immeasurable relief for their patients. The great objection to the pessary is that while the patient can remove it she cannot replace it, Gehrung to the contrary notwithstanding.

Value of Smears in Diagnosis of Gonorrhea. When dealing with inflammatory lesions of the lower genital tract it is advantageous to determine the type of infection present, but Norris and Mickelberg[2] point out that during the acute stage of the gonococcal infection the diagnosis is generally made without difficulty, as the clinical signs are more or less significant; if doubt exists, film preparations can be depended upon. During the chronic stage the clinical signs are less characteristic than during the acute stage and the examination of smears is also less satisfactory. The presence of gonococci can be demonstrated by film preparations from every case if a sufficient number of correct examinations are performed. A single negative smear examination is without significance. In such a case the chances of demonstrating gonococci are about 3 or 5 to 1 according to the skill of the examiner and even under the most favorable circumstances, positive film examinations can be obtained in only a relatively small proportion of cases. Unless safeguarded by the Gram stain, smear examinations are value-

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[1] American Journal of Obstetrics and Gynecology, 1921, **1**, 338.
[2] Journal of the American Medical Association, 1921, **76**, 164.

less and even with Gram's stain errors in diagnosis may occur since differences in the thickness of the preparations, slight overstaining, understaining, etc., may lead to extremely misleading results. Owing to the many difficulties surrounding this form of diagnosis, Norris and Mickelberg believe that unless the test is performed by one experienced in the work, its results are of no value and are often actually misleading. They believe that clinical evidence is of far greater value than staining methods, even when the latter are performed by an expert, and from a practical standpoint all cases should be regarded as of gonococcal origin until proved otherwise.

FEMALE URINARY ORGANS.

Renal Tuberculosis. The results of an analytical study of renal tuberculosis in women made by Brady[1] of the Johns Hopkins Hospital shows that in a series of 77 patients, 25, or 32 per cent of the patients complained of hematuria and in 8 of these it was the first symptom. Two patients first noticed general weakness, and in all the other cases dysuria and pyuria were the first evidences of kidney disease. The general physical examination showed pulmonary tuberculosis in 6 cases, 4 of which were active and 2 inactive. One patient developed tuberculous peritonitis two years after the removal of a tuberculous kidney. In 4 cases only a marked enlargement of the kidney was noted and in all these cases operation revealed that they were cases of tuberculous pyonephrosis. The routine gynecological pelvic examination showed the ureter to be thickened in 23 cases. This nodular thickening with tenderness of the portion of the ureter which can be felt on vaginal examination has been of great help in promptly directing attention to the probability of tuberculosis in the urinary tract. In 5 cases surgical treatment was not advised and 2 others was refused by the patient. Four of these women had tuberculosis of both kidneys; 1 with symptoms dating back eight years, the second two years, the third one year, and the fourth only eight months. One of these women died in three months, the second in six months, the third in one year, and the fourth left the hospital unimproved and has not been heard from. One woman had a unilateral renal tuberculosis with advanced pulmonary changes and in her case operation was not advised; she also left the hospital unimproved and has since not been heard of. In the 2 operable cases in which surgical treatment was refused the patients died within one year after leaving the hospital.

In 70 out of the 77 cases operations were performed. In 67 cases the kidney was removed and in 3 cases simple nephrotomies were done. The results obtained in these 3 cases are very discouraging. One woman died in three months, a second in two years, a third left the hospital unimproved and has not been heard of since. This means that 8, or 19.5 per cent of the 42 women of whom the records are complete, are now dead. These 8 patients lived, on an aver-

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[1] Bulletin of the Johns Hopkins Hospital, 1921, **32,** 13.

age, for three years after their operation. Two of the living patients are unimproved, 1 three years, the other nine years after operation. Seven may be classed as greatly improved. These 7 women are all able to carry on their daily occupations and complain of slight bladder symptoms. Twenty-five, or 59.5 per cent of these women whose present condition is known are entirely well, with an average of eleven years since operation. In this series there is 1 woman operated upon twenty-four years ago. These patients have been relieved of all their symptoms by operation and report themselves to be now in good general health. Brady has divided all the cases in which the final results are known into two classes, one formed by those women from whom only the kidney was removed and the other by those from whom as much of the ureter as possible was removed at the same time. After careful study he has been unable to show that the removal of the ureter makes any difference in the ultimate results of the operation. Approximately 19 per cent of both groups of patients are now dead, 5 per cent are unimproved, and 76 per cent are either greatly improved or well. This study, however, has shown that the postoperative sinuses of the patients on whom nephro-ureterectomies were performed healed in an average time of five months, whereas the women in whom the diseased ureters were left, drained for eleven months. From this it would appear that it is better to remove the ureter along with the kidney when the condition of the patient warrants prolonging the anesthetic the short time necessary for carrying out this procedure.

Looked at broadly, the development of our knowledge of renal tuberculosis within the last ten years has been satisfactory, according to Cabot.[1] The relative frequency of the disease, its accurate diagnosis and its satisfactory operative treatment have been developed progressively and soundly, and the improvement is nowhere better shown than in the operative mortality. Prior to 1900 the mortality for nephrectomy for renal tuberculosis was at least 25 per cent, while at the present time the mortality in the great clinics is between 2 and 3 per cent. Considering the technical difficulties of the operation of nephrectomy, the proximity of important structures including great bloodvessels, and the rather poor condition of these patients, this is a highly satisfactory showing and we might be satisfied if we did not turn our attention to the end-results. The study of results in several large series of cases taken from important clinics where results are known after a lapse of years shows that we cannot yet rest from our labor. Roughly speaking, it shows that of 97 to 98 per cent of the patients who leave the hospital after nephrectomy for tuberculosis, about 25 per cent die of urinary tuberculosis and, of this number, one-half die within the first two years and the balance within five years. In such cases, Cabot believes that they either had tuberculosis of the remaining kidney, though unsuspected, or they must have developed it very promptly after operation. There is no method now at our disposal which will enable us to diagnose "closed" tuberculosis, not the form in which closure of

[1] Minnesota Medicine, 1921, **4**, 354.

the ureter has resulted, but those tuberculous lesions of the kidney contained entirely within the renal parenchyma and communicate at no point with the renal pelvis. These cases undoubtedly exist and show a urine indistinguishable from normal. As a result of his study of the problem, Cabot believes that in a certain number of the cases we must expect tuberculosis of the remaining kidney as an unavoidable consequence of the operation and he states that there is nothing which we can do to avoid its occurrence and it must therefore be charged off to depreciation.

There is another possibility of infection occurring after operation, namely, infection of the remaining kidney as a consequence of the measures taken to arrive at an accurate diagnosis. Diagnosis of sufficient accuracy to warrant operation depends inevitably upon cystoscopy and ureteral catheterization. The majority of these patients have tuberculosis of the bladder secondary to their renal disease. In many of them the technical difficulty of the examination is great and trauma is nearly unavoidable and were we dealing with any other type of infection which was unilateral, we should be gravely conscious of the danger of infecting the remaining sound kidney. This has been largely overlooked and though it may be regarded as inevitable to accurate diagnosis, we must overhaul our methods and be sure that they expose the patients to the slightest possible danger of infection.

Technic of Nephro-ureterectomy. There are a number of pathologic conditions of the ureter and kidney, states Beer,[1] in which it is advisable to remove the kidney and ureter at the same sitting. The two essential desiderata in developing an operative technic for such a removal are: First, that the operative risk should not be materially increased by the addition of the ureterectomy to the nephrectomy; and second, that every means should be employed to avoid opening the channels involved so as not to infect the extensive retroperitoneal wound. In other words, an aseptic nephro-ureterectomy must be done. It is perfectly feasible to do the latter by the usual technic of a very long incision beginning at the last rib and extending obliquely forward in front of the anterior-superior spine and thence downward toward the external ring. This gives the necessary exposure for a complete and aseptic operation, but it is much too extensive an operation and fails to meet the first desideratum.

The operation which Beer has developed and which he believes meets all requirements begins by placing the patient in the usual lateral position and the kidney is exposed as in an ordinary nephrectomy. The ureter and pelvis are free from the vascular pedicle, which is securely tied. Then the ureter is bluntly freed (care being taken to avoid tearing the peritoneum) as far down as the fingers can reach. This is usually possible as far as the level of the crossing of the large iliac vessels; at times the dissection may reach even lower. In this dissection, the kidney may be dislocated to the upper recess in the depth of the wound, or it may be brought out of the wound altogether to produce tension on

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[1] Journal of the American Medical Association, 1921, **77**, 1176.

the ureter and facilitate dissection. The level of the iliac vessels having been reached, a long and heavy silk traction ligature is placed on the exposed lower ureter in the depth of the wound. If the kidney has been delivered it is replaced in the wound, and the wound is protected with pads while the patient is lowered from the kidney bridge, the silk ligature being brought out over the patient's abdomen so that, during the next step of the operation, it is ready to serve the operator in the rapid identification of the pelvic ureter. Then the patient is turned almost on his back and a small incision, along the outer border of the rectus muscle through its sheath, as for an extraperitoneal uretero-lithotomy, is made. By intermittent traction on the heavy silk ligature, the ureter is rapidly recognized and freed from its extraperitoneal bed down to the bladder, where, between two ligatures, it is severed either with a cautery or with a phenolized knife; then by further traction on the silk ligature, the freed ureter is delivered from the lumbar wound with the kidney attached, the upper ureteral channels remaining completely closed throughout the operation. The small anterior incision is rapidly closed in layers with a small rubber dam drain in the lower angle. Having protected this second incision with gauze dressings, the patient is again rolled on his side, the kidney wound inspected to be sure that there is no oozing, and the lumbar wound closed in layers with tube or dam drainage, as indications suggest. Beer performs this type of operation rather than the ordinary nephrectomy in (1) neoplasm of the ureter or kidney, especially papillary growths, (2) tuberculous kidney with marked stricture formation in the lower ureter with or without empyema of the ureter, and (3) impacted stone in the lower ureter associated with extensive hydronephrosis and hydroureter, with or without secondary infection.

Treatment of Pyelitis. Based upon an experience of 200 cases of renal infection, Kretschmer[1] is of the opinion that the use of vaccines does not enter into the routine treatment of pyelitis. Despite the fact that the internal administration of drugs was employed as a routine, their value seems somewhat doubtful. Of the various methods of treatment at our command, undoubtedly the one that leads the list, so far as efficiency is concerned, is pelvic lavage. The question has been raised whether the desired results are produced by pelvic lavage or by instrumentation, namely ureteral catheterization. At times one sees that after a single ureteral catheterization for diagnostic purposes in patients who have a well-marked infection of the renal pelves, the pyuria disappears as does the infection. This clinical observation is not a new one; it has been noted by various observers and has been the strong point of argument of those who object to pelvic lavage. While it is true that occasionally these infections clear up after a single cystoscopy and ureteral catheterization, Kretschmer believes that this is not the only factor or that too much importance, as a therapeutic measure, should not be attached to it.

These arguments may be met with the statement that in some of these cases of colon pyelitis that require a large number of instillations to ob-

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[1] Surgery, Gynecology and Obstetrics, 1921, **33**, 632.

tain the desired result, the repeated passage of ureteral catheters does not render the urine free of pus and bacteria. In his work he uses only one drug, namely silver nitrate, for in the early part of the work silver nitrate was used, and because of the extremely gratifying results obtained, its use has been continued. The amount of silver nitrate used should be governed by each individual patient and depends upon the size of the renal pelvis. In the average case from 8 to 10 cc were used. In cases in which a slight degree of dilatation of the pelvis is present, it stands to reason that larger amounts can be used. A precautionary measure to follow is not to overdistend the kidney pelvis, a measure which precludes the causing of pain and renal colic. If possible, pelvic lavage is carried out twice a week, or every five days, the treatment being continued until the urine is sterile and free from pus.

In treating cases of pyelitis in childhood, it is advisable to use a solution of silver nitrate of $\frac{1}{2}$ per cent strength, the amounts used varying from 1 to $3\frac{1}{2}$ cc, and depending in part upon the size and age of the child. In adults, a 2 per cent solution has been used as a routine. This may appear to some to be a rather strong solution of silver nitrate to inject into the kidney pelvis, yet Geraghty has recommended silver nitrate of the strength of 5 per cent. As a final word, it should be remembered that lesions of the abdominal viscera which may be factors in contributing to relapses or rendering this treatment inefficient must be recognized and subjected to appropriate treatment. Special stress must be laid upon giving the proper attention to lesions of the gastro-intestinal tract.

Carcinoma of the Kidney. As a result of his investigation into the literature of cancer of the kidney, together with his personal experience, Pilcher[1] states that there are three primary facts to be considered, as it is invariably one or more of these that first impels the patient to seek the physician. In their relative frequency of occurrence they are: (1) Hematuria, (2) pain, and (3) tumor. Hematuria occurs in approximately 60 per cent of the cases of tumor of the kidney and holds good both for carcinoma and hypernephroma. It may occur as a symptomless hematuria and occur either continuously, or what is more commonly the case, intermittently for months or even years. The character of the hemorrhage is in many cases quite profuse but transient and not of much severity in the earlier stages. Its presence is of the greatest aid, however, when occurring at the time of examination, as its origin can then be definitely localized. The presence of microscopic blood is of questionable value, as the errors in technic in obtaining it through ureteral catheters are so many and so easily and unintentionally committed, and other more definite findings so simply obtainable that but very little weight should be attached to this finding other than corroborative, and when found in passed urine it has no value whatever. The character of the pain complained of is not at all diagnostic of tumor of the kidney, as it varies not only in character, but also in its intensity and duration, in each instance being dependent upon its etiologic factor. Thus, one may have the colic of engagement of a stone or that accompanying the

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[1] Annals of Surgery, 1921, **73**, 301.

passage of a blood-clot; again, the distention of the tumor causing pressure and local congestion gives the dull ache frequently complained of. Similar sensations occur from the frequency of concomitant hydro- or pyonephrosis. Peripheral pressure may cause neuralgic radiations to almost any part of the abdomen; lumbago or muscular rheumatism are terms most commonly used to describe it.

Probably the one single fact that we have at our disposal upon which one may base the most accurate diagnosis of renal tumor, is the pyelo- gram. Frequent instances have been encountered, however, where this has been impossible owing to the impermeability of the ureter, either from stricture or from involvement of the tumor growth itself. The technic of its accomplishment is rendered safe and symptomless by allowing a 25 per cent solution of sodium bromide to distend the renal pelvis by gravity—the deformity noted may be of varying type, the most usual is the so-called "spider leg" appearance due to the retraction of the calyces into the cortex. The second most frequently found deformity is the splitting up of the pelvic shadow into irregular and disconnected streaks, probably due to incomplete occlusion of the normal cavity by invasion of it by the irregular tumor masses; much may also be inferred from lateral or mesial deviation or displacement of the shadow of the pelvis from pressure upon it or dislocation of it by the tumor. Renal functional tests are of doubtful value and should be interpreted with caution. The prognosis is very serious even in the most favorable cases, not only because of the usually advanced condition of the growth before it comes to operation, but there is a tremendous operative mortality—between 30 and 50 per cent.

The conclusions which Pilcher draws from his study of the subject are that carcinoma of the kidney may develop from either the epithelium of the pelvis or from that of the renal tubules and its inception is apparently due to the presence of an irritating factor, as stone, infection, or stasis. The neoplastic tissue seems to develop not at the point of irritation, but peripheral to the round-cell inflammatory reaction, one process merging into the other. Cystoscopy is absolutely essential in every case of hematuria to ascertain the source of the bleeding since it is not a symptom which allows of procrastination in determining its etiology. If from either or both kidneys, a pyelogram should be made, if possible, while exploratory operation should be performed if there is any question of the diagnosis.

Treatment of the Multiple Renal Calculi. It is a pleasure to record the conservatism expressed by Geraghty, Short and Schanz[1] in regard to the proper disposition of cases of multiple renal calculi. They state that when multiple stones are scattered throughout the kidney substance, and when, to attain any possibility of a total removal, a complete nephrectomy would be necessary, such a kidney should be left undis- turbed. If the symptoms are such, either because of infection or pain that relief is necessitated, a nephrectomy should be done, provided of course, the condition of the opposite kidney does not contraindicate this

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[1] Journal of the American Medical Association, 1921, **77**, 901.

procedure. Complete nephrotomy is an operation attended with grave risk because of the danger of secondary hemorrhage, which may occur as late as the third week. Because of the necessity of suturing the kidney to control hemorrhage, extensive destruction of renal tissue occurs and a functional impairment occurs which might not be produced by the renal calculi in a long period of time. If the nephrotomy is done in the presence of infection, it will result in even greater damage to renal tissue, for to the destruction resulting from the mattress suturing is added that of impaired drainage of infection in the areas included in the suture. The probability of incomplete removal of multiple calculi, particularly in those cases having many small stones, adds to the difficulty of securing a good functional result with this operative procedure in this type of case.

Finally, persistent urinary fistula is a not uncommon sequela and probably results from the subsequent dislodgment of small calculi overlooked at operation which result in obstruction requiring another operation for its correction. They do not advise against the removal of multiple calculi in all cases since there are certain cases in which the stones are of a size and occupy a position which renders feasible their removal through a pyelotomy, through several small nephrotomy incisions or a combination of the two. Careful preliminary consideration of the number, size and position of the calculi, their relations to the pelvis and calyces and the presence or absence of an extrarenal pelvis, will usually enable one to determine the feasibility of removal by a conservative procedure. Occasionally in cases of multiple calculi in which under ordinary circumstances operation would be inadvisable, a calculus may be dislodged into the pelvis or ureter, resulting either in great discomfort or in a serious destruction of the kidney. Under such conditions the obstructing calculus should be removed and no attempt made to remove the multiple calculi in the kidney substance. This should hold particularly true if the other kidney has a low functional value.

There is another group of cases in which the kidney is literally filled with calculi, frequently of considerable size. In the majority of these cases the kidney will be found to be a mere shell with an extremely low function. If the condition just cited is unilateral and the opposite kidney is of good functional value, a nephrectomy is usually indicated. When, however, the renal lesion is bilateral, as not infrequently happens in this type of case, experience has shown that removal of these calculi, through a nephrotomy has not led to any appreciable improvement in function, as the destruction is of such extent as to render impossible any regeneration. When a pyonephrosis intervenes, usually the result of a stone getting into such a position that it seriously interferes with drainage of the kidney, surgical interference is justified even in extreme cases. It is advisable in these cases to control hemorrhage if possible by packing around a large rubber tube rather than to use sutures, as a better functional value will be maintained. In order to pack successfully in such cases, the nephrotomy incision should not extend from pole to pole, as usually all of the calculi can be removed through a large incision in the midportion of the kidney.

The treatment of staghorn or branching calculi deserves special consideration. They are practically never the cause of renal colic and seldom give rise to more than slight uneasiness or discomfort in the kidney region, and their existence is frequently an accidental discovery. The function of these kidneys is surprisingly good as a rule, even in the presence of infection. The removal of these calculi always necessitates a complete nephrotomy, and the renal impairment resulting will usually be greater than would be produced by the stone over a period of years. Furthermore, in the removal of the calculus, small or even fair sized fragments may be overlooked, which, if they do not result in the production of a permanent urinary fistula, will certainly lead to the reformation of calculus. These kidneys should rarely be operated on, and when operation is necessary, nephrectomy should usually be done.

Ureteral Transplantation. There are occasions arising from time to time in the practise of surgery when a satisfactory method of transplanting one or both ureters will be of inestimable value to both the patient and the surgeon concerned. The principal force to be dealt with in implantation of a duct into the intestine is static intra-intestinal pressure and similarly, Coffey[1] states, the essential mechanical principle necessary to the uniformly successful implantation of the ureter is that the ureter shall be made to run immediately under the loose mucous membrane for a distance, before entering the lumen of the intestine. The technic of the operation which he has perfected begins by locating and ligating the ureter with linen or silk. It is then cut in two above the ligature and the edges caught and held with mosquito forceps, while one wall of the ureter is split down with a pair of scissors. A linen suture is passed through the split end of the ureter so as to include about one-half of it, and tied. The linen thread is thrown around the other half and tied. The loose ends are threaded into two needles. By this method the full strength of the ureter is retained for traction, while the opening is maintained by the slit.

The end of the ureter is wrapped with gauze while the intestine is prepared for its reception, which is done as follows: The part of the intestine desired is picked up and an incision made down through the peritoneal and muscular coats, including submucous tissue. The muscular layer is loosened from the mucosa with the point of a knife until the mucous membrane pouts out through the incision. This incision should be about one inch or more in length. Then, five or six sutures are passed which pick up the peritoneal and muscular coats on each side of the incision. The suture at the upper end of the incision is tied as a control suture. The intermediate intestinal sutures are lifted up on the flat handle of an instrument as they cross the incision. Now the intestine is brought down close to the end of the split ureter and the two needles carrying the threads (traction sutures) on the end of the ureter are passed beneath the four or five intestinal sutures and through the stab wound in the mucous membrane into the intestinal lumen and out through the intestinal wall $\frac{3}{4}$ of an inch farther

[1] Surgery, Gynecology and Obstetrics, 1921, **32**, 383.

along the intestine, and $\frac{1}{8}$ to $\frac{1}{4}$ of an inch apart. By making the tension on these threads and at the same time pushing the intestine toward the
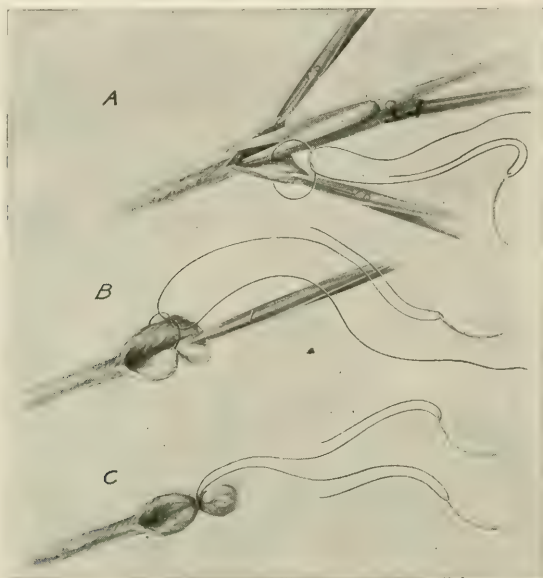
Fig. 4.—Method of preparing suture.   (Coffey.)

ureter, it is drawn beneath the intestinal sutures through the stab wound into the intestinal lumen.   The two ends of the threads on the ureter are tied on the outside, thus anchoring the end of the ureter on the inside of the intestine at this point.   The intestinal sutures are then tied.   After
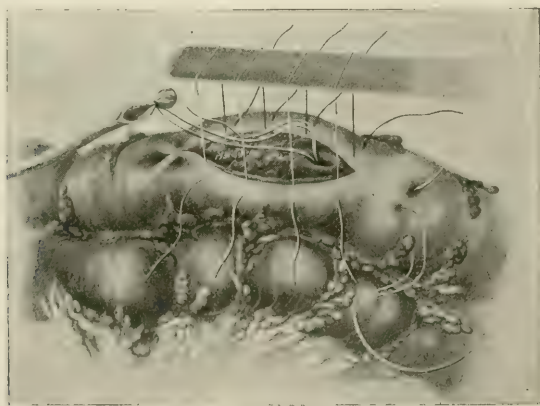
Fig. 5.—Transplantation of ureter into the intestine.   (Coffey.)

this operation the ureter lies just beneath the mucous membrane, which has been loosened for about $\frac{3}{4}$ of an inch of its course, so that it slides easily

in its new channel. It is therefore necessary to tack the ureter to the peritoneum of the intestine near its point of entrance by two or three fine linen or silk bloodvessel sutures. Care should be used to take only the outer coat of the ureter in the bite of these sutures. Thus, practically all of the steps of the operation are completed before the intestinal mucosa is penetrated and no sutures penetrate the lumen of the ureter. The traction suture at the end of the ureter within the intestine and the two or three anchor sutures fastening the ureter to the intestinal peritoneum are the only means of retaining the ureter in place.

Operative Treatment of Bladder Neoplasms. Although the electrical cauterization of bladder neoplasms has been successfully employed for many years by Beer[1] since he introduced it to the profession, he has repeatedly urged that this method of treatment should not be employed in malignant growths or benign growths (*a*) that are not readily accessible, (*b*) that surround the sphincter and bleed so that a thorough treatment is impossible, (*c*) that are so numerous that the bladder is studded with tumors (papillomatosis), and (*d*) those cases that for one reason or another are intolerant and cannot be regularly cystoscoped. In cases of the above mentioned types, operation must be employed and the technic which has given Beer the best results is as follows. After irrigating the bladder it is emptied so that when it is opened the wound is not flooded with fluid containing tumor cells, and the patient is placed in the Trendelenburg position and a suprapubic incision is made. The bladder is exposed and freed extraperitoneally and the urachus is doubly clamped and cut. After the bladder is well freed down to the trigone, the perivesical space is packed off with gauze pads and the bladder is incised either through its anterior, posterior or lateral wall, depending upon the position of the growth. Sponging within the bladder should be reduced to a minimum. When the growth is exposed, it is immediately cauterized *in situ* with the electric cautery and every suspicious spot is treated similarly, remembering that a too extensive cauterization, is preferable to a too superficial one. If the bladder wall is infiltrated, a wide cautery resection of this area is indicated. If a ureter is involved in the infiltrated area, it is left attached until this area is resected and is then cut away from the resected portion at a distance from the growth and is implanted into a healthy portion of the bladder just before the bladder wounds are sutured. The use of clamps with teeth, such as the Kocher clamps, which produce minute perforations in the bladder wall, thus possibly producing implants, should be avoided throughout the operation. In order to further prevent the possibility of bladder implants, the incision which opened the bladder is carefully seared with the cautery and then the whole wound is filled with alcohol for about five minutes, the bladder being allowed to slip back into its bed so that its cavity, as well as the protective gauze, is exposed to the effects of the alcohol which it is hoped will coagulate any potential cell implants which have broken away during the various manipulations. The bladder is then sponged dry and closed, after making provision for suprapubic

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[1] Annals of Surgery, 1921, **73**, 72.

tube drainage. In closing the bladder, a layer of plain catgut sutures is used to infold the charred edges of the incision and over this a layer of chromic gut is applied to support the first layer. The abdominal incision is closed in layers with rubber dam drainage to the bladder both above and below the tube which enters that organ.
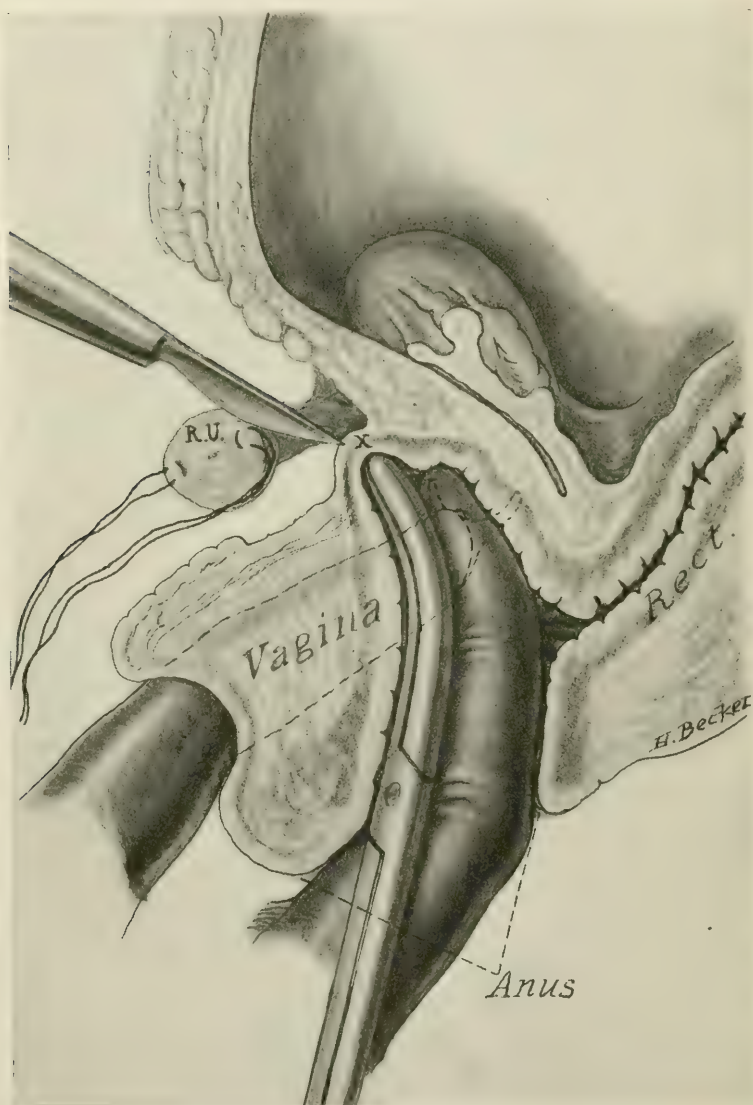
Fig. 6.

Exstrophy of the Bladder in the Female. In looking up the literature on exstrophy of the bladder, Burk[1] was unable to find a single instance

[1] Annals of Surgery, 1921, **73**, 100.

of operative cure of such a condition in the female subject by the extra-peritoneal method and therefore he presents the details of a case of this congenital anomaly in a female which he has succeeded in curing. The technic which he followed in this case began with the introduction of catheters in the ureters for about six inches. This served a twofold purpose, (*a*) as guides, giving definite knowledge of the position and course of the ureters, and (*b*) as conductors of urine from the ureters, rendering the operation field free from contamination. Beginning at the muco-cutaneous border of the bladder, he made a $2\frac{1}{2}$ inch incision through the skin and fat in the median line, down to the rectus fascia and the fascia was split the whole length of this incision. Beginning at the posterior wall of the bladder at the lower end of the incision, with gauze on the index finger, separation of the bladder from the peritoneum was accomplished with little difficulty. The bladder was then com-pletely freed from the abdominal wall and the dissection was continued down to the ureters which were easily distinguished on account of the catheters which were previously inserted. After freeing the bladder and isolating the ureters for about $1\frac{1}{2}$ inches, the bladder was split in the middle line down through the trigone. Beginning at this point he incised the bladder circularly about $\frac{1}{4}$ of an inch away from the ureter meatus, therefore making a button or rosette of bladder with the meatus in the center. In this manner the blood supply as well as the sphincter action of the ureter outlet was preserved. This was performed on each side, of course. Then two mattress sutures of catgut were inserted into each rosette, leaving the ends long. At this stage of the operation it was necessary for an assistant to dilate the anal sphincter and introduce the index finger into the vagina and the middle finger into the rectum. A long forceps was passed up into the rectum, the middle finger of the assistant acting as a guide, and pushed up to meet the operator's finger from above. Between the operator's finger and the assistant's middle finger were rectal wall and pelvic fascia. A small incision was made over the tip of the forceps and the latter pushed up through the rectum to grasp the long ends of catgut attached to the bladder rosette con-taining the ureter opening. The catgut with the ureter was then drawn through the opening made in the rectum and at the completion of the operation the ureters hung suspended for about $\frac{3}{4}$ inch in the rectum, about 1 inch above the anal sphincter. In transplanting these lower ends of the ureters it was attempted to prevent any kinking. The remaining part of the bladder was extirpated and iodoform gauze was packed loosely down to the rectum on either side of the vagina, to act, first, to stop the oozing which was considerable, and second, to help to prevent the ureters from slipping from the rectum. The abdominal wound was closed in the usual manner down almost to the pubes, just enough opening left to permit the two gauze strips to emerge. The catgut strands hanging in the rectum, attached to the rosettes, were brought outside the anus and kept taut by adhesive plaster in order to prevent the slipping back of the ureters from the rectum and a piece of rubber tubing was then placed in the rectum.

DISORDERS OF NUTRITION AND METABOLISM; DISORDERS OF THE GLANDS OF INTERNAL SECRETION; DISEASES OF THE BLOOD AND SPLEEN.

By ELMER H. FUNK, M.D.

NUTRITION.

Newer Aspects of Some Nutrition Disorders. In a lecture before The Harvey Society, Hess[1] pointed out that although the disorders brought about by a deficiency of vitamins or accessory food factors have occurred for centuries, they must to a considerable extent, however, be regarded as typical modern disorders. He states that, viewed as a group, they are a consequence of our unnatural mode of life and peculiar civilization, of the growth of immense cities housing millions of people who are dependent on perishable foodstuffs transported from a great distance. To even a greater extent, they are the product of countless ingenious methods devised mainly to render food stable—drying, heating, the addition of preservatives—most of which accomplish their objects, but incidentally rob the food of one or more of its essential constituents. In a measure, these nutritional disturbances are a consequence of the supreme domination of the bacterial point of view, of the ever-present dread of infection and solicitude to protect ourselves against contaminated foodstuffs. This fear has led to the demand for a more or less complete sterilization of foods, and to a preference for foodstuffs whose unsullied whiteness lends them the appearance of purity—as in the case of polished rice and highly milled flour. Hess also states that although the current view associates deficiencies of the various vitamins with specific disorders, for example, with beriberi or with scurvy, it is likewise true that clear-cut disorders should not be regarded as the most common or important result of food deficiencies. It should be realized that a lack of these essential food factors generally does not bring about typical pathologic states, but obscure alterations of nutrition, ill-defined functional disabilities, which cannot be characterized or even recognized as disease. It is such incomplete, larval forms of the deficiency disorders to which physicians will have to address themselves. Nor should the domain of the deficiency disease be restricted to the narrow confines of disturbances brought about by a lack of vitamins. In a broader sense, it includes malnutrition due to an insufficiency of any food constituent which is essential to normal metabolism. The people of the Central Empires, for example, as the result of a great lack of meat, milk, cheese and eggs, were com-

[1] Journal of the American Medical Association, 1921, **76**, 693.

pelled to subsist during the war on a dietary which was deficient in phosphoric acid as well as in one or more of the vitamins. Hess's paper is so full of important material concerning our modern conception of nutritional disorders in their various relations that the reader should consult the original article and read it as a whole. Some of the points which he mentions will be dealt with in the following pages.

Vitamins. We recognize two general types of vitamins—the water-soluble and the fat-soluble. The water-soluble group includes: (*a*) the original antineuritic vitamin of Funk; (*b*) the growth-promoting vitamin; (*c*) the yeast-stimulating vitamin; and (*d*) the antiscorbutic vitamin. Besides these there are some suggestions being put forth which tend to show that there are other water-soluble vitamins. As to the fat-soluble vitamins, there has been described, so far, but the one form—designated by McCollum as fat-soluble A.

In McCarrison's book entitled *Studies in Deficiency Disease*, which has appeared during the past year (1921), it is pointed out that absence of food leads to starvation; absence of the vitamins renders the food useless, and so also leads to inanition. Inanition, or starvation, is the essence of all deficiency diseases; the malnutrition so produced renders the tissues an easy prey to infectious agents, so that conditions due secondarily to the latter may cause further symptoms to be super-imposed on those due to failure of the food supply. The remarkable effect on the adrenal body, which hypertrophies, endocrine insufficiency, involving other ductless glands, and gastro-intestinal disturbances are preëminent. It is no doubt true that the absence of individual vitamins will produce different effects, and it is useful to be able to speak of the vitamins A, B, and C, but underlying all, starvation is at the root of the matter.

Cramer, Drew and Mottram[1] emphasize that vitamins are essential for the maintenance of life of a highly differentiated animal as a whole, but not necessarily, or probably, of its individual cells. There is, however, one tissue which is specifically and profoundly affected by the absence of vitamins from the diet, namely, the lymphoid tissue. In mice and rats kept on a diet completely free from vitamins, there is a great atrophy of the lymphoid tissue, which is obvious even to the naked eye. The spleen is shrunk to a narrow ribbon; the thymus, which even in adult rats and mice remains relatively a large organ filling the upper part of the thorax and covering the base of the heart, becomes so small as to be hardly visible. The Peyer's patches, which are prominent in normal animals, are difficult to identify with the naked eye. Microscopically, these organs, especially the spleen, are found to contain very few leukocytes. The ordinary lymph glands may not be macroscopically smaller than normal, but under the microscope are found to be almost bare of lymphocytes. They consist almost entirely of endothelial cells and large, empty lymph spaces. The blood picture, as shown by a differential count, shows a reduction in the number of lymphocytes and an increase in the leukocytes. This

[1] Lancet, 1921, **200**, 963.

condition of the lymphoid tissue is practically identical with that produced by exposure to roentgen rays and radium. These agents, if given in appropriate dosage, not only have the same effect as regards the lymphoid tissue, but they also produce the same general effect on the animals—loss of weight and death in a state of emaciation. Incidentally, it may be recalled that in this condition there are also degenerative changes in the seminiferous tubules of the testicles similar to those observed in avitaminosis. Why two such apparently dissimilar causes should produce the same effects is a problem which the authors quoted above propose to investigate further.

In a later paper, Cramer, Drew and Mottram[1] report their studies on the function of the lymphocyte and of lymphoid tissue in nutrition, with special reference to the vitamin problem. Their conclusions from these studies are as follows:

Absence of the water-soluble B vitamin from the diet leads, in rats and mice, to an atrophy of the lymphoid tissue throughout the body and to a lymphopenia in the circulating blood. The polymorphonuclear leukocytes are not affected. Absence of the fat-soluble A vitamin does not lead to an atrophy of the lymphoid tissue and there is no lymphopenia. Absence of the water-soluble B vitamin leads to characteristic nutritional disturbances, such as loss of weight, emaciation, subnormal temperature, which may be designated by the term "marasmus." No such marasmus results from withholding the fat-soluble A vitamin.

The lymphopenia established by withholding the water-soluble B vitamin is rapidly abolished by the administration of the water-soluble B vitamin and *pari passu* with it, the concomitant marasmus. A permanent lymphopenia and, associated with it, an atrophy of the lymphoid tissue throughout the body, can also be induced by exposure of rats to sufficient doses of roentgen rays or radium. Such animals then also develop a condition of marasmus similar to that observed when the water-soluble B vitamin is withheld. Since the functional disturbances in the lymphoid tissue produced by two such widely different agencies lead to the same nutritional disturbances, it is concluded that the lymphocytes play a part of fundamental importance in the nutrition of the body. Other evidence points to the conclusion that they are concerned in the absorption and assimilation of food from the intestine.

Further evidence of the existence of an intimate relationship between the functional activity of the lymphoid tissue and the general nutrition of the organism is afforded by the fact that an abundant supply of the water-soluble B vitamin has a favorable effect on the development of lymphoid tissue and the number of lymphocytes, and associated with it on the general nutrition of the animal. There is, further, the clinical experience that disturbances of lymphoid tissue are of special significance in infancy and are there frequently associated with nutritional disturbances.

[1] Lancet, 1921, **201**, 1202.

The conception that vitamins—and the B vitamin in particular—are necessary for the life of every individual cell is criticised by Cramer and his co-workers. They say that this vitamin is necessary for the maintenance of life of a highly differentiated animal, not because its presence is necessary for the life of all the cells of such an animal, but because its presence is necessary for the normal functioning of lymphoid tissue. In other words, the term "deficiency diseases" is, like the term "vitamin" a misnomer. These diseases have their origin, like other diseases, in specific lesions. These lesions may be induced by different agencies of which a deficiency in vitamins is only one.

Wright[1] studied the effect of the water-soluble B vitamin on the appetite in animals. He concluded that vitamin B acts by facilitating the efficient carrying out of the functions of the intestinal canal. The main effects produced by the absence of the vitamin—*i. e.*, diminished food consumption, loss of weight, and ultimate death—are due to intestinal stasis and the absorption of toxic bodies which results therefrom.

The studies of Cramer, Drew and Mottram[2] suggest therapeutic possibilities of B vitamin apart from the obvious one in conditions of marasmus associated with a lymphopenia. An abundant supply of the water-soluble B vitamin stimulates the functional activity of the lymphoid tissue and increases the number of lymphocytes in the circulating blood. The administration of this vitamin may, therefore, have a favorable influence in the course of infections in which the defence depends on the activity of the lymphocytes. The old-fashioned administration of yeast to persons suffering from boils is perhaps an empirical application. Conversely, it may be possible to inhibit the excessive production of lymphocytes in lymphatic leukemias by withholding this vitamin. Another more obvious application which would appear to follow is that persons undergoing treatment by roentgen rays or radium, or working with these radiations, should receive an ample supply of this vitamin in their diet. As pointed out further,[3] carbohydrate and fat metabolism seem dependent upon a proportionate amount of B factor per calorie ingested. This connection suggests the administration of B vitamin in cases of diabetes to assist the utilization of sugar. The addition of cod-liver oil or butter (fats rich in A vitamin) to a diet deficient in B vitamin has been shown to cause loss of weight and ill-health, while an increase in amount of B vitamin led to assimilation of the fat with renewed health and growth. Cases of marasmus in infants which had failed to put on weight by the usual treatment, began to grow directly they were given extra B vitamin. Hess reported several years ago that, although yeast, which is rich in B vitamin, apparently possessed little or no value as an antiscorbutic, it proved an excellent stimulant to growth in infants; he showed graphs of infants of under 1 year, $1\frac{1}{2}$, and 2 years of age, who had maintained an almost constant weight for weeks or months in spite of various changes in diet, and showed an immediate and continuous rise after the ad-

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[1] Lancet, 1921, **201**, 1208.   [2] Ibid.   [3] Ibid.

ministration of autolyzed yeast. In some cases the appetite was stimulated, but in others there was a prompt response though the total food intake was not increased. That the yeast had a favorable effect on the digestive processes was shown not only by the increase in appetite, but by the improved character of the stools.

The Lancet editorial[1] points out further that the chief source of B vitamin in our food is the seeds of cereals and other plants, but the factor is removed from cereal seeds in the process of milling. Sugar, sago, and other farinaceous products are lacking in B factor, meat and fish are poor, offal and eggs, in comparison, rich. Vegetables and milk contain small amounts. The quantity in the foodstuffs is scarcely sufficient to balance the large carbohydrate consumption of white flour in our diet, unless eggs, fruits, and vegetables are eaten in great quantities. The products richest in B vitamin are the germ of cereals and yeast. Germ, as such, is not consumed by humans (except in whole meal bread) and the yeast used in baking bread is not sufficient. Yeast contains B vitamin in great concentration, and palatable preparations made therefrom can compensate for the lack of B vitamin in other foods. No ill-effects have been ascribed to too great a consumption of foods rich in B vitamin, and it is likely that certain cases of vague ill-health would be improved by the consumption of additional quantities of B vitamin. There is here a promising field for clinical research.

Milk is a valuable food, not only because of its high calorie content, but because it contains all the vitamins. Rosenau[2] points out that milk is not equally rich in all vitamins, but contains these essential accessory dietary factors in variable amounts. The antiscorbutic value of milk depends almost entirely on the fodder of the cow. Human milk, no doubt, also varies with the nature of the mother's food, and in some instances is deficient, owing to eccentricities of diet or to poverty. The quantity of vitamins in plants probably varies with the soil in which they are grown, and animals in turn suffer by lack of, or profit by, richness of vitamins in plant foods. Milk is usually rich in all three vitamins. It is usually rich in fat-soluble A, contains an abundant amount of water-soluble B, and a variable, but ordinarily sufficient, quantity of antiscorbutic vitamin. Therefore, it protects against all of the known deficiency diseases. It has long been known that the effect of heat on vitamins varies with the reaction and other factors. Most vitamins are more readily affected by heat in an alkaline medium than in an acid one. Fortunately, most foods are acid. Milk is acid from the time it leaves the udder. With regard to the effect of heat upon antiscorbutic vitamin, it has been shown that the duration of the heating process is of greater importance than the degree of temperature to which the food is subjected. Dry milk may retain its antiscorbutic virtue in spite of drying, canning and ageing, especially if well packed and hermetically sealed. It loses its potency after it is exposed to the air. Canned milks and dried milks, then, retain the

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[1] Lancet, 1921, **201**, 1228.
[2] Boston Medical and Surgical Journal, 1921, **184**, 455, abstract, Journal of the American Medical Association, 1921, **76**, 153.

fat-soluble A and water-soluble B vitamins in almost their original potency. The only vitamin in these preparations that may be affected is the antiscorbutic vitamin. The amount of this in canned milk will vary with many factors, primarily, the amount in the original milk, and, secondarily, on the process of heating and evaporation, with special reference to oxidation.

Reference to the wide distribution of the vitamins in the various foodstuffs was made in these columns in past years. A table of the commoner foodstuffs showing the distribution of their accessory factors is contained in the *Journal of the American Medical Association*, 1921, lxxvii, 571.

A current comment[1] of a practical nature is that the accessory food factors are so well distributed throughout the dietary of modern man that, generally speaking, the individual who uses ordinary judgment in selecting his food is in no danger of suffering from a deficiency of any of the three factors.

Nutritional Keratomalacia. The relationship between this type of corneal disease and malnutrition in infants was first noticed by W. Mackenzie in 1857, and was confirmed by subsequent writers, among whom we may mention Holmes Spicer who, in 1892, observed the condition in England only among artificially-reared infants, who had a diet lacking in nitrogenous elements. He also noted that it was not uncommon in countries where nursing mothers practised long fasts. (Quoted from Editorial, *Lancet*, 1921, cci, 814).

Ross[2] records 4 cases in children fed almost exclusively on condensed milk, a food high in carbohydrate value, relatively low in fat and protein, and probably deficient in the fat-soluble A factor. The prognosis of keratomalacia is grave in infants, but improves greatly above the age of one year. Death results from nutritional disturbance, and the eye lesion is an indication that this is far advanced. Three of Ross's patients died, 2 from bronchopneumonia. Treatment consists in supplying a sufficient quantity of animal fat which contains the fat-soluble A factor. If breast milk is not available, cow's milk should be employed. The use of cod-liver oil should be begun immediately in doses of 5 minims three times a day.

From the experimental side come the observations of Osborne and Mendel who found, in their nutritional studied on rats, that these eye changes in keratomalacia or xerophthalmia occur only in the absence of vitamin A in the diet. Among 1000 rats, those fed on a diet free from vitamin A showed these pathological eye phenomena, while of other rats fed so as to be but poorly nourished, on food containing vitamin A, not a single animal showed keratomalacia. That this condition is not the consequence of simple malnutrition is further shown by the fact that the eye symptoms usually begin before there is a decrease in body weight. In 61 cases, 33 animals showed the phenomenon before there was any loss of body weight. A daily addition of 0.1 gm. of butter fat or vegetable oil (extract of plants, grass, alfalfa, spinach),

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[1] Journal of the American Medical Association, 1921, **77**, 561.
[2] American Journal of Diseases of Children, September, 1921.

caused the diseased state of the eye to disappear in two weeks, and a local improvement of the condition in cases where death could be prevented.

The pathology of the ophthalmia associated with the dietary deficiency in the fat-soluble A vitamin was studied by Wason.[1] The pathological changes are characterized by hyalinization or necrosis of the outer layer of corneal epithelium, exudation of serum and cells into the epithelium and stroma, and a proliferation of bloodvessels and fibroblasts. In advanced cases invasion of the anterior, and occasionally of the posterior, chamber results. Bacterial invasion is secondary, and the type and virulence of the organisms of secondary infection determine, in part at least, the course of the disease. The degree to which restoration is possible depends on the extent of the secondary injury. The primary etiologic factor, however, in the ophthalmia of rats on deficient diets, is the lack of fat-soluble vitamin A.

To refer again to the xerophthalmia as it affects human beings, it is interesting to recall its occurrence in Denmark where, in 1917, during the submarine blockade, the prevailing doctrine was that of Hindhede to the effect that fat was a dispensable foodstuff. Lusk[2] states that there was then no knowledge in Denmark of the American work. Bloch[3] describes how the Danish children grew to be weaklings, without appetite, under height and under weight for their ages, and they developed xerophthalmia. These conditions were cured by rationing butter and selling it to the poor at low prices. Administration of whole milk and cod-liver oil was also effective. Ten gms. of cod-liver oil, given twice daily, cured the xerophthalmia in eight days except in cases in which its administration had been too long delayed to save the eyesight. Lusk states that one can hardly cite a more clear-cut example of the benefits conferred upon a people from knowledge of experimental biological science.

Famine Dropsy, or Hunger Edema. "Famine dropsy is a form of edema associated with bradycardia, polyuria and asthenia which occurs as the result of prolonged underfeeding. It is unattended by albuminuria, cardiac dilatation, or neuritis. It affects by preference men performing hard physical labor, whose food has a low calorie content (800 to 1200), these calories being embodied in a large fluid diet which comprises 15 per cent or more of indigestible cellulose with very little fat and a maximum daily allowance of 50 gms. of protein."

This definition is given by Nixon[4] who discusses briefly the history of the disease. It is interesting to know that reference to famine dropsy may be found in the literature of the Greeks. Our present day interest in the disease is with regard to its occurrence in the famine areas of Central Europe and other parts of the world where food deficiency exists. The main exciting cause is prolonged underfeeding. The ingestion of fluid in large quantities is a contributing factor. The

[1] Journal of the American Medical Association, 1921, **76**, 908.
[2] Physiological Reviews, 1921, **1**, 523.
[3] Journal of Hygiene, 1921, **19**, 283.
[4] Pennsylvania Medical Journal, October, 1921, 43.

diagnosis, according to Nixon, rests upon a syndrome of four cardinal symptoms: Edema, polyuria, bradycardia and asthenia. A known insufficiency of diet will also assist in arriving at a diagnosis. It must not be forgotten, however, that food deficiency may arise not only from an inadequate supply of foodstuffs but also from an inability to assimilate and make use of the food ingested, so that it remains an open question whether diseases of the alimentary tract, such as diarrhea or dysentery, may not produce an identical dropsy. Moreover, in the present state of our knowledge, it is impossible to say whether the so-called "inanition dropsies," seen in such diseases as phthisis and cancer, are examples of the same condition.

The diagnosis is only justifiable in the absence of certain symptoms which frequently accompany other forms of dropsy: Cyanosis, cardiac dilatation and albuminuria. Beriberi, scurvy and pellagra may cause a dropsy which is not famine dropsy, but these diseases may exist concurrently. Hookworm disease presents great difficulty in differential diagnosis, but the presence of profound anemia with considerable eosinophilia will suggest the necessity for careful examination of the feces for occult blood and the hookworm ova.

The death rate in persons over forty years of age has been estimated at 18 per cent, in children between three and four years old at from 22 to 33 per cent. Uncomplicated cases begin to recover within forty-eight hours if kept warm in bed with an increased diet: but relapses are common when a patient first gets up and exerts himself. It may be some weeks before a patient can get up without a return of edema. The latest researches show that an adequate protein is no less essential to the dietary than an adequate supply of calories. The diet at first must be light and easily digested. Small quantities must be given as in any case of starvation. The amount of liquid and of common salt should be limited. Coexisting diseases demand special attention. Relapses of diarrhea often cause great trouble and retard recovery. Cod-liver oil has proved a most valuable remedy. The prevention of the disease is solely a matter of diet.

Hunger Osteomalacia. Toward the end of 1918 a condition with symptoms comparable to those of the earlier stages of osteomalacia was prevalent in Vienna. Roentgen ray photographs showed in some cases osteoporosis and in a few instances spontaneous fracture occurred. Dalyell and Chick[1] described the onset, symptoms and course of the disease as follows:

The initial symptom was difficulty in walking, owing to pain in the tarsal and metatarsal bones, generally accompanied by edema of the feet and ankles. The edema, when present, subsided after some weeks, but without diminution of pain on walking. The lumbar and sacral regions were next affected, and stooping or walking was accompanied by severe pain in these areas, of an intense and persistent nature. Thoracic symptoms developed later, with pain on compression of the ribs, progressing from lower to upper ribs; pain was often felt also on

[1] Lancet, 1921, **201**, 842.

coughing or deep breathing. Arms, shoulders, and hands were not so often affected, and face symptoms were present only in the most severe cases. The muscles were not painful when handled, showed neither wasting nor other deformity, and their contractile force was not diminished. It was therefore unlikely that the whole muscle was involved in the existing lesion. The nerve reflexes were normal, and there was no evidence of peripheral neuritis nor of damage to nerve trunks, so that it was improbable that the symptoms of the disease could be due to nerve involvement only. The association of tetany was not infrequent. The degree to which bones were involved in the region was difficult to determine. The sensitive areas were limited to the points of attachment of certain muscle groups, *e. g.*, adductor muscles of the thigh, lumbar muscles, etc. The disease usually progressed until the patient was completely immobilized in bed, and sucumbed to intercurrent disease (usually pulmonary) or to starvation, which was not impossible in Vienna in 1918-1920.

The occurrance of this disease in Vienna during the period of greatest deprivation and the beneficial effect of improved diet without any other form of treatment suggested its dietetic origin. Dalyell and Chick found that the mere adding of extra calories in the form of carbohydrates produced little improvement. Recovery followed, however, the addition of either cod-liver oil, butter, oleomargarine containing 80 per cent of animal fat, or olive oil. The beneficial influence was in the order named, cod-liver oil being the most effective. Some of the severer cases did not improve until cod-liver oil was given. The therapeutic response to the fats corresponded roughly with their fat-soluble A vitamin content. The remission of symptoms in summer and their relapse in winter are due to varying supplies of vitamin A. The increase in Vienna of rickets in children suggests that the two disorders may be due to the same cause.

Hume and Nirenstein[1] made a comparison of the treatment with cod-liver oil and plant oil. Most of the patients made progress, but some of the patients on plant oil (subsequently identified as belonging to the rape oil group and containing phosphorus) had to be transferred to cod-liver oil, and some of those on cod-liver oil had to have the dose increased before good progress could be made. These observers concluded in a provisional way that the cure of the disease was due to the addition of fat-soluble vitamin A, rather than of fat as fat to the diet. They regard the relation of hunger osteomalacia to the osteomalacia of pregnancy as quite uncertain.

How Much Fat Shall we Eat? This is the title of an editorial[2] from which I wish to quote at some length. Before the shortage of foods entailed by the world-wide conflict, an American consumed, on the average, $3\frac{1}{2}$ ounces of fat a day; an Englishman, $3\frac{1}{8}$; a German, $2\frac{1}{3}$ and a Frenchman $1\frac{1}{2}$. During the progress of the war the Interallied Scientific Food Commission recommended the adoption of 75 gm. ($2\frac{5}{8}$ ounces) of fat for the average man each day as a desirable minimum

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[1] Lancet, 1921, **201**, 849.
[2] Journal of the American Medical Association, 1921, **76**, 656.

of fat to be secured for human consumption. This represents about 700 calories, or, approximately, one quarter of the average daily energy requirement of each person involved. Some of the physical ills which visited the underfed peoples of the war were charged to the shortage of fats in the ration. In a previous paragraph, mention was made of the relation of hunger osteomalacia and the dietetic restriction of fats. That fat is a potent food is obvious from a consideration of its fuel value alone. A pound of fat yields two and one-fourth times as much energy as does a pound of any other nutrient utilized by man. A study of the dietary habits of different races at once suggests, however, that the apparent dependence of persons on fats may have culinary motives as well as purely physiologic reasons. The Japanese, for example, habitually eat little fat. But it is the habit of both Europeans and Americans to use considerable fat, both on the table and in cooking. Accordingly, the query, "How much fat do we need?" Without knowledge of the importance of vitamins, for example, all earlier attempts to study the role of fats of the diet by feeding them in varied proportions as isolated substances inevitably failed. A diet rich in fat might bring nutritive failure as readily as one poor in this foodstuff, the untoward outcome in either case being due to a neglected and unrecognized further factor in the food mixture. Again, the presence of fat in the diet might bring beneficial results because it was the chance carrier of vitamin A, associated with some fats more than others. Recent controversies regarding the necessity for fats in the diet fail to emphasize adequately the distinction in the significance of fats as sources of energy and as carriers of vitamin and of lipoids, regarding the role of which we are still largely uninformed.

Drummond and Coward[1] studied experimentally the nutrition and growth of rats on diets devoid of true fats. The rats grew from weaning to maturity on diets deprived as far as possible of neutral fats, and showed normal development and behavior. More deaths were encountered among the animals on the fat-free diets than among those receiving fats. It would appear that neutral fats are, from a purely physiological standpoint, dispensable constituents of a diet, provided the other foodstuffs supply a sufficiency of the vitamin frequently found in association with neutral fats. The real value of fats as convenient sources of energy is obvious.

The Pirquet System of Nutrition. Considerable discussion has occurred both in and out of the literature concerning the applicability of this system to American conditions. As formulated by Pirquet, it is essentially a method of feeding based on scientific principles applicable to the rationing of large groups. In Austria alone 300,000 children and in Central Europe 1,500,000 children have been fed by this method. Carter[2] describes it clearly and in detail. There are three features of the Pirquet system: First, the nutrition unit, or *nem;* second, the method of estimating the nutritional requirements, or *pelidisi;* and third, the physical examination. As Carter states, Pirquet felt that a nutritional

[1] Lancet, 1921, **200**, 698.
[2] Journal of the American Medical Association, 1921, **77**, 1541.

unit based on the food value of 1 cc of milk was preferable to the calorie, which suggests nothing to one unaccustomed to thinking in terms of physics. To the milk unit Pirquet applied the term *nem* (nutrition, —element-milk). The nutritive value of any food can be readily expressed in nems simply by comparing its food value with that of milk. For example, gram for gram, the value of sugar is six times that of milk. It would take, therefore, approximately 17 grams of sugar to equal 100 cc of milk. Carter gives a table of the nem value of foodstuffs, and shows with what simplicity diets can be prepared according to this system.

In the estimation of the nutritional index, or *pelidisi*, Pirquet uses the following formula:

$$\frac{10 \text{ times the weight}}{\text{Sitting height}^3} = 100 \text{ per cent.}$$

Pirquet believes that there is a direct relationship between the food requirements of the individual and the absorptive surface of the alimentary canal. He demonstrated that the measure of this absorptive surface in square centimeters is equal to the figure arrived at by squaring the sitting height. Thus, a child with a sitting height of 50 cm. would have an absorptive surface of 2500 sq. cm. Pirquet applied the term *siqua* to the square of the sitting height. He also found that the maximum quantity of milk absorbable in twenty-four hours was 1 cc per sq. cm. of absorptive area; or 1 nem per sq. cm. The maximum of food absorbable in a child of 50 cm. sitting height would be 2500 nems. Pirquet found, however, that the maximum food intake on this basis would overtax the digestive system. He estimated that the irreducible minimum or the needs of the individual for basal metabolism as three-tenths of the maximum. He also estimated that the growing individual needs one tenth of the calculated maximum for purposes of growth, that he must have another tenth for the maintenance of his reserves of body fat; that he required still another tenth to meet the demand of moderate exercise and a further tenth if he is one whose activity is unusual. The sum of these fractions provides the physician with a basis for calculating the nutritive needs of the child and for writing his prescription. For example, the prescription would read, 0.5, 0.6, 0.7 or, unusual cases, 0.8. For these figures, Pirquet has given the name "decinemsiqua" (written DnSq). To further amplify: Consider the same child whose sitting height is 50 cm. As stated, the square of 50 cm. (2500 sq. cm.) gives a figure which is about the same as the number of square centimeters of the intestinal "absorptive surface." This figure also represents the "maximum" number of nem which can be utilized by this surface. The child needs, to meet the demands of its basal metabolism, three tenths of the "maximum," 2500 nem, which is 750 nem; for its growth, one tenth of the "maximum," or 250 nem; for fat reserve, one tenth, or 250 nem; for moderate activity, one tenth, or 250 nem more, should be added. It is apparent, therefore, that this child would require 1500 nem, or six tenths of the

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"maximum." If this child should become very active, another one tenth could be added to bring his total daily intake up to seven tenths, or 1750 nem.

The word, *pelidisi*, was coined by Pirquet (*p*ondus, *de*cies, *li*near, *di*vided by *si*tting height). In actual practice, the pelidisi of a well-nourished, normal child is very close to 100 per cent. An obese child may go up to 110 per cent. Thin children run between 88 and 94 per cent. The thinnest we have observed in this country or in Austria was 85 per cent. Generally speaking, a child with a *pelidisi* between 95 and 100 per cent may be said to be well nourished. An adult, however, with a *pelidisi* below 100 per cent is undoubtedly undernourished. At 104 or 105 per cent, he is overfed and the intake should be reduced. In the American Relief Administration's feeding, the line is drawn at 94 per cent. If food were plentiful, Pirquet would probably insist that the limit be gradually raised to 98 or 100 per cent.

The third feature of the Pirquet system is the method of reporting in a standardized way the result of the physical examination of the child. As Carter points out, Pirquet classified the results of the examinations under four headings—sanguis (blood), crassitudo (fat), turgor and muscularis. He chose the vowel *a* to indicate normality and *e, i, o, u* as symbols to designate the degree of deviation of these tissues above or below normal. In this way a new word was evolved, one that would represent the physical status of the child. Eventually "sacratama" came to mean the physical examination.

SACRATAMA

	Sanguis (blood).	Crassitudo (fat).	Turgor (water).	Muscularis (muscle).	
i	Si	cri	ti	mi	Greatly increased.
e	Se	cre	te	me	Moderately increased.
a	Sa	cra	ta	ma	Normal.
o	So	cro	to	mo	Moderately decreased.
u	Su	cru	tu	mu	Greatly decreased.

Index 3–2–1–0.

Further to simplify the formula (it is sometimes difficult to remember without consulting the chart what "so-cre-to-ma," for example, means), an index was formulated: 3-2-1-0. To illustrate: If a child were slightly anemic and moderately thin, but of good turgor and muscle tone, his classification would be "so-cro-ta-ma." It is apparent that there are two points off normal, so a circle is thrown around the 2. If, on the other hand, he were particularly well muscled and he were classified "so-cro-ta-me," he would have two points below normal and one point above; the difference would be 1, and a circle would be thrown around this number.

It is a common observation that there is a direct relationship between the *pelidisi* and the sacratama. When the *pelidisi* is around 90 per cent, the sacratama is likely to be three points off normal; if the *pelidisi* is near 95 per cent, the sacratama will probably be one or two points off normal. A normal *pelidisi* almost invariably accompanies a normal sacratama.

In the application of the Pirquet system to the school children of certain selected districts of San Francisco, Carter found an average of 53 per cent with a *pelidisi* of 94 or under, and 7 per cent with a *pelidisi* of 100 or over. From these figures it is evident that supplemental feeding is necessary and Carter believes that the Pirquet system can be applied with advantage.

Horwitt[1] considers that the introduction of the Pirquet system in America at the present time is undesirable, since it would serve to focus attention on schematic methods instead of individualization. One child may have tuberculosis, another anemia, a third may be chronically fatigued, etc. Weymouth[2] questions the reliability of the standards set by the Pirquet system, which finds so many children undernourished, as in the San Francisco observations of Carter. Pirquet's figures must be revised in order to fit American conditions. Using Hasting's figures as a standard he found a *pelidisi* of about 94.25 normal, or 100 per cent, for American children. The corrected ratio would be as follows:

$$\frac{10.52 \times \text{weight}}{\text{Sitting height}^3} = 100.$$

Weymouth considers the Pirquet system as a practical method of dealing with the general question of child nutrition. When corrected according to American standards it allows of a rapid and reasonably accurate application to large groups of children.

The *food requirements of the child* have recently been reviewed by Holt and Fales[3] who found that the requirements for growth are greatest during the period when growth is most active, namely, during the first year and during adolescence. The requirements are nearly uniform from the fourth to the tenth year. Food requirements during the period of adolescence are higher than is generally assumed. The total daily caloric requirement of children during adolescence exceeds by nearly 1000 calories the requirements of the adult of the same sex under conditions of moderate activity. Underweight children require more calories than those of average weight of the same age. Overweight children require fewer calories than the average. These observations of Holt and Fales interpret the taking of more food by the average child as compared to the average adult as representing the response to a real physiologic need.

Nutrition Work Among American School Children. Reference was made last year in these columns to the nutrition work in the public schools of Chicago by Rich. A continuance of that work has resulted in an increased percentage of gains over those previously obtained. In Chicago, approximately 500 children have been included in these nutritional classes, and in the last half-year period recorded they have gained 121 per cent in weight and 64 per cent in height, in excess of the normal gain. From the gross percentages of gains in weight and height

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[1] Journal of the American Medical Association, 1921, **77**, 1756.
[2] Ibid., 2080.
[3] American Journal of Diseases of Children, 1921, **21**, 1, also Editorial, Journal of the American Medical Association, 1921, **76**, 728.

has been deducted the normal increase, and Rich considers that with an underweight of 10 to 30 per cent below normal, these children could not possibly have gained even that amount had they been left to themselves. Rich comments further, that the finding of 50 per cent of the school children below normal in height and weight for age, or in weight for height, is evidence that the country-wide interest which has been aroused in the subject of undernourishment has come none too soon; but unless that interest is wisely directed, it will do as much harm as good. It should be primarily, the problem of the medical profession, of the pediatrician, and particularly of the family physician. For the benefit of the coming generations, it might very wisely be given great emphasis in the teaching of the pediatric departments of our medical schools.

Calcium Metabolism. Calcium and magnesium are antagonistic to sodium and potassium. Small amounts of calcium prevent the stimulating action of sodium in experiments on isolated muscles; hence Loeb[1] once remarked that we are indebted to the calcium concentration for the fact that our muscles do not constantly twitch. Kramer, Tisdale and Howland[2] have confirmed the previous work of Howland and Marriott on the concentration of inorganic phosphorus in the serum of individuals the subjects of active tetany, the relationship between the sum of the univalent cations, sodium and potassium, and the divalent cations, calcium and magnesium. In infantile tetany, the inorganic phosphorus of the serum shows a marked variation. The ratio $\frac{Na \text{ and } K}{Ca \text{ and } Mg}$ is increased. This is almost wholly due to a decrease in the concentration of calcium. The increased irritability of the neuromuscular mechanism, which is the essential phemonenon in infantile tetany, is due to the diminution of the concentration of calcium in the serum.

Denis and Talbot[3] studied the calcium content of 119 samples of blood from children, irrespective of the diagnosis, and found a maximum figure of 13.5 and the minimum 1 mg. per 100 cc of blood plasma. In 22 normal adults the maximum was 12.1 and the minimum was 7.2 mg. and the average was 10 mg. of calcium per 100 cc of plasma. In 28 cases of rickets, 7 in the acute and 21 in the convalescent stage, some gave calcium values distinctly below the normal, but as some of these were suffering others illnesses, such as pneumonia, no definite conclusions could be drawn. In tetany, the calcium content of the serum was extremely low. The administration of calcium chloride 25 grains three times a day, in 2 cases gave a marked increase in the blood calcium in 1 case. Associated with this increase was the disappearance of the symptoms and apparent cure. In cases of convulsions not due to tetany, the blood calcium was very low. This was especially true in epilepsy. In 25 cases of lobar pneumonia, bronchopneumonia and

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[1] Quotation from Editorial, Journal of the American Medical Association, 1921, **77**, 2062.
[2] American Journal of Diseases of Children, 1921, **22**, 431.
[3] Ibid., January, 1921.

acute bronchitis, the blood calcium was very low. After the crisis it rose somewhat. There was no calcium excretion during the febrile stage, but there was after the crisis.

Meysenbug and McCann[1] found that in experimental tetany the reduced serum calcium is not due to a lowering of the diffusible as contrasted with the non-diffusible form. The proportion between the two remains constant in the presence of a reduced total. In two cases of rickets, with serum calcium of 9.0 and 7.6 mg. per hundred cc, the percentage of diffusible calcium was found by von Meysenbug and McCann to be between 58 and 70 per cent, within the range found in normal subjects. In normal men and dogs, Meysenbug[2] found the diffusible calcium to comprise from 60 to 70 per cent of the total serum calcium. Varying the carbon dioxide saturation of the serum between 17 mm. mercury tension and 62 mm. does not alter this percentage.

Healy[3] reports from clinical experience how sodium bicarbonate given in large quantities by bowel after operation may upset the normal relations between the sodium, potassium, calcium and other ions in the neuromuscular tissues, resulting in the symptoms of tetany. Among 7 such patients there were 4 deaths and 3 recoveries. The 3 recoveries occurred in patients who were given calcium lactate by mouth.

Jeppsson and Klercker[4] observed a child of seven years who invariably developed tetany with carpopedal spasm whenever it was given sodium phosphate by the mouth. It showed no tendency thereto at other times. This confirms the view that the spasmogenic substance in milk is the whey, and that only the salts in the whey, and probably only the alkaline phosphates, are responsible for the symptoms we call spasmophilia. Their researches indicate that children with latent spasmophilia are not affected by whey which has been deprived of its phosphates. The excessive ingestion of alkaline phosphates upsets the relations between the sodium, potassium, calcium and other ions, resulting in spasmophilia. The calcium and phosphorus content of the serum in relation to rickets will be discussed under this disease.

The blood content of calcium and phosphoric acid in normal children was studied by Jones and Nye[5] who summarized their findings as follows:

The alkali reserve of plasma and the distribution of calcium and the various compounds of phosphoric acid in the blood were studied in thirty-four normal children whose ages ranged from four weeks to fourteen years.

From these studies, it appears that the blood corpuscles are richer in all types of phosphoric acid compounds than plasma. The amount of unknown phosphoric acid in plasma is negligible, if any, while in corpuscles it averages approximately 70 per cent of the total.

In general, the values for boys averaged slightly higher than those for girls. The lipoid phosphoric acid content of corpuscles averaged

[1] Journal of Biological Chemistry, 1921, **47**, 541.   [2] Ibid., 1529.
[3] American Journal of Obstetrics and Gynecology, 1921, **2**, 164.
[4] Zeitschrift für Kinderheilkunde, 1921, **28**, 71.
[5] Journal of Biological Chemistry, 1921, **47**, 321.

17.7 per cent higher in boys than in girls, while the plasma value in boys was 16.6 per cent higher than that in girls. The inorganic phosphoric acid content of corpuscles showed the greatest percentage variation of all the phosphorus compounds of the blood.

The average calcium content of corpuscles was found to be slightly less than that of the plasma, the values in mg. per 100 cc being as follows: Whole blood, 9.4 mg.; corpuscles, 8.7 mg.; plasma, 10 mg. A relation between the calcium and phosphoric acid contents of the blood is not apparent.

The CO_2 combining power of the plasma averaged 51.8 volumes per cent in thirty-two children. No relation between the alkali reserve and the concentration of calcium and phosphoric acid in the blood can be established.

The human body[1] contains about 1 per cent of the element calcium, or a total of nearly 2 pounds, most of which is represented by calcium phosphate deposited in the skeletal structures. The daily "waste" has been estimated to exceed 0.5 gm., so that the normal supply would not be exhausted in less than two or three years if it were entirely available for physiologic uses. Pregnancy and lactation have long been recognized as conditions in which there is an unusual need of lime for the growth of the fetus, on the one hand, and, on the other, for the production of the lime-bearing milk of the mother. The daily requirement for the development of the fetus at four months, for example, is at least 150 mg. of calcium; 1 liter of milk includes approximately 200 mg. of this element. It is quite conceivable, therefore, as has been pointed out, that shortage of calcium may become a reality if the diet is not well selected; for meats and cereals, fats and sugars—all of which enter so largely into present-day rations in this country—are at best very inadequate sources of lime.

Another editoral[2] commenting upon the work of Telfer[3] on the influence of free fatty acids in the intestinal contents on the excretion of calcium and phosphorus states, in part, as follows: "Despite the conflicting opinions, there is at present sufficient evidence to make it probable that the calcium factor in the food plays an important part in determining to what extent phosphates can be absorbed. When there is a great abundance of calcium and magnesium in the intake, earthy phosphates are most likely to appear in abundance in the excrement. Telfer studied the metabolism of infants in whom the existence of congenital atresia of the bile ducts resulted in the failure of absorption of the fatty acids arising in the digestion of fats in the alimentary tract. A similar effect can be observed in obstructive jaundice. The non-absorption and persistence of an excess of fatty acids in the intestine are associated with a modification of the normal excretion of calcium and phosphorus. The calcium is found in the feces as soaps in large excess over the normal. The phosphorus, which normally is excreted by the bowel as tricalcium phosphate, is liberated from combination

[1] Editorial, Journal of the American Medical Association, 1921, **77**, 625.
[2] Journal of the American Medical Association, 1921, **77**, 1496.
[3] Biochemical Journal, 1921, **15**, 347.

with calcium and is absorbed and eliminated by the urine. The degree to which the normal excretion of calcium and phosphorus can thus be varied is shown to depend on the concentration of the free fatty acids in the intestinal contents. This is evidently one of many ways in which the perplexing interrelations between two elements essential for the organism can be influenced."

Alkaptonuria. Gibson and Howard[1] report a case of this interesting anomaly of metabolism of which there are not more than 70 cases in the literature and only 11 have been reported from America. The condition is characterized by the presence in the urine of alkapton or homogentisic acid. The urine, on exposure to the air or on the addition of alkali, turns brown or even black. It reduces copper solutions, but does not yield to the fermentation test, does not reduce alkaline bismuth solutions and does not rotate polarized light. An ammoniacal solution of silver nitrate is quickly reduced by it in the cold. Lastly, when a dilute solution of ferric chloride is added to the urine, drop by drop, a deep blue color appears for a moment, as each drop falls, until oxidation is complete.

Alkaptonuria is more common in males than in females and in a number of reported cases the familial tendency is evident. As a rule there is no inconvenience experienced by the patient, except, possibly, the staining of the underclothes by the urine. Occasionally there is dysuria. It is often not recognized until the patient submits to a life insurance examination and the applicant is rejected as a diabetic.

Gibson and Howard, in discussing the pathogenesis of this "inborn error of metabolism," as Garrod calls it, state that it consists of a failure to complete the catabolism of the aromatic fractions of the proteins, tyrosin and phenylalanin. The tyrosin and phenylalanin of both the food and tissue proteins are concerned. During fasting the output of homogentisic acid is diminished, but is not arrested. A diet rich in proteins greatly increases the output, and when tyrosin and phenylalanin are given by mouth to an alkaptonuric an almost corresponding quantity of homogentisic acid appears in the urine. On the other hand, these amino-acids, when taken by normal persons, are destroyed and the benzene ring broken up. The quantities of homogentisic acid excreted by different alkaptonurics are singularly uniform when the nature of the diet and ages of the patients are allowed for. This amount varies from 3 to 6 gm. in twenty-four hours, though rarely 16 gm. and even 18 gm. have been found. Garrod states that there is reason to believe that the error is in all instances complete and maximal in degree. In order to prove metabolically that their patient was one of alkaptonuria, Gibson and Howard administered a constant diet of 70 gm. protein, 83 gm. fat, and 253 gm. carbohydrate; no meat or soup. The homogentisic acid and total nitrogen excretion were determined and the effects of tyrosin added to the diet observed. The characteristic increase in homogentisic acid was observed to follow the tyrosin ingestion. It was Garrod who pointed out that in alkap-

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[1] Archives of Internal Medicine, 1921, **28**, 632.

tonurics, the conversion of tyrosin and phenylalanin into homogentisic acid is so complete that the ratio of homogentisic acid to the total nitrogen in the urine tends to be constant and the same for all cases. The homogentisic acid amounts to 40 or 45 per cent of the total nitrogen figure.

Rombach[1] records a case of alkaptonuria which was discovered during a life insurance examination. There was present also a dark blue staining of the cartilages, especially the ear, which was distinctly visible through the skin. In other words, ochronosis was present. Gibson and Howard state that a small proportion of the cases of alkaptonuria (24 cases up to 1919) are associated with ochronosis or blackening of the cartilages and fibrous tissues and pigmentation of the skin. Alkaptonurics, with an associated ochronosis, may reveal during life pain, swelling and deformity of one or more of the larger joints of the extremities or of the small joints of the hands—a condition termed by Osler ochronotic arthritis.

Rickets. ETIOLOGY AND TREATMENT. At the present time, according to Sweet,[2] there are two different schools of thought on the subject of the etiology of rickets, namely, the dietetic and hygienic—the former considering that a defective diet is the cause of the disease, and that lack of fresh air, sunshine and exercise is only a contributing factor which increases the severity of the disease but never causes it if the diet is satisfactory; the latter claim that rickets is directly due to a hygienic defect.

Mellanby[3] has recently summarized five years' work on observation of 400 puppies. This author believes that the antirachitic factor which ricket-preventing substances are presumed to contain is the same as fat-soluble A vitamin. There are various experiments attesting the activity of food factors in the etiology of rickets. Thus, protein has a definite antirachitic effect, while carbohydrate tends to promote the development of rickets. Further experiments bear on the question of exercise in its relation to rickets, and the author compares its influence to that of protein in preventing or modifying the disease. Thus an antirachitic factor, "probably identical with the fat-soluble vitamin," together with sufficient calcium and phosphorus in the diet, are considered factors of first importance in preventing rickets: meat and exercise assist in prevention. Restriction of any of the four factors named or excess of carbohydrate food promotes the development of rickets.

On the other hand, Paton and Watson[4] state that in puppies under laboratory conditions a liberal allowance of milk fat neither prevents the onset of rickets nor cures it when it has developed. Pups kept largely in the open air may escape the development of rickets on an intake of less than 1 gm. milk fat per kilo of body weight. With scrupulous care as to cleanliness it is, at least sometimes, possible to rear pups free of

[1] Nederl. Tijdschr. v. Geneesk., March 5, 1921.
[2] British Medical Journal, December 24, 1921, 1067.
[3] British Medical Research Council, Special Reports, Series No. 61, quoted editorially, Lancet, 1921, **2**, 1233.
[4] British Journal of Experimental Pathology, 1921, **2**, 75.

rickets in the laboratory on an intake of only about 0.5 gm. milk fat per kilo of body weight, along with bread, provided that the diet affords an adequate supply of energy. The energy value of the diet, however supplied, quite apart from the presence of any hypothetic antirachitic factor in milk fat, would seem to play a part in controlling the development of rickets, but that it is only a contributory part is shown by the development of rickets in pups with a high energy intake if confined in the laboratory without scrupulous care as to cleanliness.

Hess[1] and his co-workers, by reason of their dietary experiments on children, are opposed to the vitamin theory, and noting, as most other observers of the disease have done, that rickets is most active in winter and tends to improve in spring and summer, suggest that lack of sunshine is an importnat etiologic factor in rickets. Sun-baths in spring and ultraviolet rays in winter have a curative effect on infants suffering from this disease.

Feer[2] says that the *mountain sunlight* has an almost specific effect in the cure of rachitis. Sweet's[3] conclusions are based on a study of rickets as it occurs in Australasia, where in former times, its supposed absence was used as an argument against the dietetic origin of the disease. It does exist, however, in a mild form and is by no means uncommon. The benign character of the disease in Australasia is probably due to the climatic condition which allows of a maximum outdoor existence. On the other hand, the primary etiologic factor seems to be a diet deficient in fresh animal food, probably suitable protein, or to a disturbed digestive condition which prevents the assimilation of the same. Sweet further concludes that the metabolic changes in rickets are due secondarily to a deficiency of secretion of one or more of the endocrine organs and probably chiefly of the thymus gland. He does not believe that the deficiency of fat-soluble A vitamin in the diet has been proved. Hess says that the fact that when on some milk 25 per cent of the children will get rickets, while the others under the same conditions will show no sign of the disease, shows that there is some individual idiosyncrasy. If we adopt the dietetic theory of rickets, we must go further, and be able to explain why a similar diet given to three infants is capable of producing atrophy in one, rickets in another, while a third child remains in good health.

Hess, McCann and Pappenheimer[4] found that, although animals receiving a diet complete except for a lack of vitamin A invariably failed to grow and in due season were likely to die, the skeletons showed no gross changes whatever. Microscopic examination presented definite signs of a lack of active osteogenesis, but in no instance lesions resembling rickets. Hence these investigators concluded, in conformity with their previous experience in regard to infantile rickets, that if the diet is otherwise adequate, lack of vitamin A does not bring about rickets.

Powers, Park, Shipley, McCollum and Simmonds,[5] in an interesting

[1] Archives Pediatrics, July, 1921, Journal of the American Medical Association, 1921, **77**, 312, and Journal of the American Medical Association, 1921, **77**, 39.
[2] Schweizerische medizinsche Wochenschrift, 1921, **51**, 437.   [3] Ibid.
[4] Journal of Biological Chemistry, 1921, **47**, 395.
[5] Journal of the American Medical Association, 1922, **78**, 159.

study on experimental rickets, found that sunlight effectually prevents the development of rickets in the rat. In their experiments, a diet was employed which at room light regularly gives rise to a disease in its essential features identical with rickets as seen in human beings. The diet was high in calcium, low in phosphorus and was insufficiently supplied with fat-soluble A. In other respects, it was well constituted. Eighteen rats were placed on the diet. Twelve were exposed to sunlight for a total of two hundred and forty-two hours over a period of sixty-two days. Six were kept under conditions of ordinary room light as control animals. The control rats, killed with ether at the end of sixty days, all showed rickets. The rats exposed to sunlight, killed coincidentally, remained without exception entirely free from rickets. The absence of the lesions of rickets was confirmed by histologic examination. The beneficial effects of the sun's rays were not limited to the skeleton, since the animals underwent a general improvement as well. These same observers note, however, that the exposure to the sun's rays did not entirely compensate for the defects in the diet. The animals remained undersize; the bones, though completely calcified, remained thin. Though the sunlight did not alter the defects in the diet, it permitted the animals to thrive to a limited extent in the presence of them. Powers and his co-workers conclude, therefore, that the sunlight in some way raises the efficiency of the body cells. It enables the organism to put into operation regulatory mechanisms which otherwise would have been inoperative or ineffectual. The effects of sunlight and of cod-liver oil on the growth and calcification of the skeleton and on the animal as a whole, seem to be similar, if not identical.

In the treatment of infantile rickets, Hess and Unger[1] practise exposure to the sun's rays for a half hour or several hours, varying the period of treatment according to the intensity of the sun and the sensitiveness of the skin. The legs, arms, trunk and face are in turn exposed. It is remarkable how well infants under one year of age react to this outdoor treatment, if carried out gradually and under careful supervision. Five infants, 3 between six and twelve months, and 2 between twelve and eighteen months of age, were treated in this manner. The exposures obviously could not be carried out with regularity, but experience showed that daily treatment is not essential. In 1 of the cases which responded most favorably, the patient could be given the sunlight treatment only on seven days between April 3 to 19; during this period exposure was given for a total of twenty-five hours. In every instance there has been marked improvement in the rickets, as evidenced by the calcification of the epiphyses noted by means of the roentgen ray. The alteration resembled that which follows the administration of cod-liver oil, and, in 1 instance, occurred thirteen days after heliotherapy was begun. The general condition of the infants was also benefited, as were other signs of rickets, such as beading of the ribs and flabby musculature. In 1 case, calcification of the epiphyses of both wrists was evident, when as yet but

[1] Journal of the American Medical Association, 1921, **77**, 39.

one arm had been exposed to the sun – evidence that the action of the rays is systemic and not local.

The use of *cod-liver oil*, which over many years has been considered almost a specific in the treatment of rickets, now rests upon a rational basis, since it has been shown that it favors the retention in the body of calcium. Hess,[1] in his Harvey Lecture, states that its unequaled value in the prevention and cure of rickets is hardly realized. The marked success attending the use of cod-liver oil in districts where rickets is rampant has convinced Hess that it would be feasible to rid a locality of the disease by the use of this oil. Thus, there are approximately 125,000 children in New York City between the ages of three and fifteen months, the period of greatest susceptibility to rickets. If we estimate generously, Hess writes, that the families of from one-quarter to one-third of these children are unable to purchase cod-liver oil, and if we agree that the development of rickets may be prevented by giving a teaspoonful three times a day, then, at the present cost, rickets could be practically abolished in that city by the expenditure of about $100,000 a year. This, Hess concludes, is merely one of many instances in which the community does not get the full benefit of our medical knowledge.

Zilva and Muira[2] have shown that the crude unrefined cod-liver oil may be 250 times richer in fat-soluble A than butter, and much superior to the refined preparation of cod-liver oil which the public prefers, the refining process destroying partially the vitamin content.

In two patients studied by Phemister, Miller and Bonar,[3] the administration of *phosphorus* caused equally prompt healing of rickets as compared with those treated with cod-liver oil. Further observations were deemed necessary, however, to clear up this point. The experimental work of Shipley, Park, McCollum and Simmonds[4] suggests that the phosphate ion in the diet may be a determining factor for, or against, the development of rickets. They maintain that if the phosphate content of the diet is sufficiently high, a deficiency of vitamin A cannot cause rachitic changes in the skeleton. Hence such a deficiency cannot be the sole cause of rickets. Sherman and Pappenheim[5] caused rickets in young rats and then, solely by the substitution of 0.4 per cent. secondary potassium phosphate (K_2HPO_4) for a small part (one-seventh) of the calcium lactate present in this diet, completely prevented the development of rickets, though no effect was produced on the body weight. This is held to prove that rickets may be induced or prevented without change in either the protein or vitamin components of the diet, and, as has been shown previously by others, that an adequate supply of calcium does not in itself protect against the disease. The protective action of the potassium phosphate is not clear, and the authors carefully guard themselves from being thought to support the view that rickets is due to a deficiency of potassium or phosphorus.

[1] Journal of the American Medical Association, 1921, **76,** 693, and Editorial, Journal of the American Medical Association, 1921, **76,** 1009.
[2] Lancet, 1921, **1,** 323.
[3] Journal of the American Medical Association, 1921, **76,** 850.
[4] Johns Hopkins Hospital Bulletin, 1921, **32,** 160.
[5] Journal of Experimental Medicine, 1921, **34,** 189.

They suggest that the quantitative relation of the inorganic ions, rather than an absolute deficiency of any one of them, may be a determining factor, and that very possibly, under certain conditions of diet in which there is an unbalanced quantitative relationship of the organic as well as the inorganic foodstuffs, rickets may develop.

Howland and Kramer[1] found in children with active rickets that the calcium concentration may be normal or slightly reduced. Findlay, Paton and Sharpe[2] found that the tissues other than bone in experimental rickets in dogs are not deficient in calcium. The calcium content of the blood in experimental rickets in dogs shows no divergence from the normal. The inorganic phosphorus of the serum in children, according to Howland and Kramer, is regularly reduced in active rickets, sometimes to an extreme degree. During the process of healing, whether occurring spontaneously or as the result of the administration of cod-liver oil, the phosphorus content of the serum gradually rises to a normal figure and often somewhat above this. Relapses are accompanied by a fall in the phosphorus-concentration of the serum. All the children under two and one-half years of age, in whom the authors found an inorganic phosphorus content of the serum of 3.0 mg. or less, have been suffering from active rickets. The problem of rickets is, as pointed out editorially,[3] evidently far more complicated than was ever suspected, but with the possibilities of direct experimental attack on it now opened by the recent studies in the nutrition of laboratory animals, the prospect of a successful solution looms large.

Of considerable clinical interest are the studies of Park and Howland[4] on THE DANGERS TO LIFE OF SEVERE INVOLVEMENT OF THE THORAX IN RICKETS. Thirty-two children were studied, of whom 22 formed the basis of their report. The average age was sixteen months, and all were colored. All were underweight and underheight. All showed clinical evidences of rickets in other parts of the skeleton in addition to the chest. The chest deformity was quite marked and often markedly asymmetrical. When inspiration takes place in the deformed chest, almost every deformity becomes intensified. In general, it may be said that every hollow, every eminence, every peculiar curvature or inequality present during expiration becomes increased during inspiration. The moment that the inspiratory effort is complete, the whole thorax snaps back into the expiratory position as if released from a spring.

The deformities and usual movements of the thorax are brought about because the bony thorax has lost its rigidity. This loss of rigidity is the direct result of the failure of calcium deposition, and, very probably, also, of resorptive processes in the bones themselves set in operation by the disease. The changes in the thoracic wall must inevitably lead to changes in the thoracic contents. When the thorax is opened, attention is immediately attracted to two striking conditions, the

[1] American Journal of Diseases of Children, 1921, **22**, 105.
[2] Quarterly Journal of Medicine, 1921, **14**, 352.
[3] Journal of the American Medical Association, 1921, **76**, 1844.
[4] Johns Hopkins Hospital Bulletin, 1921, **32**, 101.

knuckle-like enlargements at the costochondral junctions which pro-
ject a considerable distance into the thoracic cavity, and the grooves,
one on the external surface of each lung not far from the anterior border,
running in a direction from above downward, outward and backward.

When the lungs are removed from the thorax, it is seen that they
are far too small for the size of the child. The right lung is usually pro-
portionately smaller than the left. It can then be seen that the grooves
divide the external surface of each lung in such a way that roughly
one-quarter lies in front and three-quarters behind. That part of the
lung in front of the groove is for the most part emphysematous, while
that part lying behing it is generally dark bluish in color and of a firm
consistency. Obviously, it is atelectatic. It is not entirely atelectatic,
however, for interspersed with the collapsed pulmonary tissue is tissue
in a state of emphysema. Areas of lobular pneumonia are almost
always present and frequently the cut surface exudes serum, showing
the presence of edema. Hypertrophy of the heart is also present, and
the part giving evidence of it is the right ventricle.

The sequence in the development of the condition seems to be as
follows: The rachitic thorax loses its rigidity, yielding during inspiration
simultaneously at costochondral junctions and shafts. As the rigidity
of the thorax becomes diminished, the depressions at the sides, which
at first were present only during inspiration, persist during expiration.
As the bones progressively lose their elasticity, the dynamic deformity
gradually becomes static as well. Thoracic respiration is at first
slightly, later profoundly, affected. Coincident with the impairment
of thoracic respiration, diaphragmatic respiration is enfeebled. The
efficiency of each inspiration, therefore, is diminished. A compensa-
tion is attempted in an increased frequency of respiration and in an
increased force. But the greater the force applied, the greater the
collapse produced. Nature's efforts in large part defeat themselves.
The diaphragm pulls its attachments yet further inward, and the
accessory muscles draw the bones to which they are fastened out of
position without moving or giving stability to the thorax as a whole.
Owing to the progressive reduction in the size of the thorax and its loss
of power to expand, the lung begins to become atelectatic. One of
the parts early affected is that pressed upon by the costochondral
junctions. As the pathological process progresses, the atelectasis
increases; the pressure in the pulmonary circulation rises; and hyper-
trophy of the right heart follows. If the rigidity of the ribs becomes
still further impaired, a point is reached at which the disabled respira-
tory machine is just sufficient to perform its work. If, now, a slight
additional burden is put upon it in the form of an infection, it becomes
insufficient. Park and Howland state that for the comprehension of
the condition it is necessary to realize that deformity and normal thoracic
function are compatible; in other words, that the element of danger
is not the deformity but the loss of rigidity of the thoracic wall.

Scurvy. It will be recalled that Hess[1] over a year ago reviewed the
literature upon this subject and rendered certain deductions based on

[1] Scurvy, Past and Present. J. B. Lippincott Company, Philadelphia, 1920.

his own extensive observations and those of other students in this field. He pointed out that there is no etiological difference between the scurvy seen in adults and that of infants. The prevalence of the latter is far greater than generally recognized, owing to the increased use of artificial foods which are for the most part deficient in the antiscorbutic vitamin. Hess believes that infants bought up on natural milk do not contract scurvy, and he places a rather higher value on unheated cow's milk than is assigned to it by the workers at the Lister Institute. While recognizing that pasteurized and boiled milk are very inefficient, Hess holds that the value of milk is not appreciably diminished by the rapid drying method used in the Just-Hatmaker process; if so, it is a very valuable and practical substitute for raw milk. He states that there is no basis for assuming an interrelationship between infantile scurvy and rickets; scurvy, he says, will develop as rapidly when rickets is absent as when present; in practice, however, the two diseases often are present together. For prophylaxis and cure, Hess places the greatest reliance on raw orange and lemon juice or strained canned tomato. For infants of one month old, he recommends the addition of one teaspoonful of orange juice daily, believing that it is not wise to wait, as is the common practice, until the fifth or sixth month.

Givens[1] states that while text-books discussing scurvy indicate the value of fresh fruit or vegetables, they do not give their relative antiscorbutic potency. The results of the studies of Givens and his co-workers are, briefly, as follows: Raw orange juice, tomatoes, cabbage, potatoes, apples, and bananas are good antiscorbutc agents. Of these foods, the content of antiscorbutic vitamin is greatest in orange and least in bananas. Cooking tends to diminish the amount of the antiscorbutic accessory. Orange juice and tomatoes can be dried so that they retain a significant amount of their original vitamin content. Canned tomatoes are good antiscorbutic agents.

The factors which enter into the conservation or destruction of the antiscorbutic vitamin continue to be the subject of study by various workers. Bassett-Smith[2] draws attention again to an efficient dried preparation of lemon juice which he hopes will be useful for special expeditions of a naval character. He has tested, experimentally, the tablets prepared by the method which he described[3] previously and found that they retained their efficiency over twelve months. The tablets are prepared by a special process of evaporation at room temperature.

The concentration of orange juice to a dry state, while still retaining its antiscorbutic properties, has been demonstrated by McClendon[4] and his co-workers and by Givens and Macy.[5] Hess[6] has pointed out the destructive effect of oxidization on the antiscorbutic vitamin. The

[1] Pennsylvania Medical Journal, June, 1921, 629.
[2] Lancet, 1921, **201**, 321.
[3] Ibid., 1920, 1, 1102 and **2**, 997.
[4] Journal of Biological Chemistry, 1921, **46**, 9; ibid., 10.
[5] Ibid., 11.
[6] Proceedings of the Society for Experimental Biology and Medicine, 1921, **18**, 143.

addition of hydrogen peroxide, for example, to raw milk, brings about a loss in the antiscorbutic vitamin. The harmful effect of "ageing" may be due to the deleterious action of slow oxidization. The same destructive process occurs in the various manipulations of the foodstuffs, and may explain the difference in antiscorbutic potency of milk heated in open pans or hermetically sealed bottles. Zilva[1] found that bubbling air at ordinary temperature through an antiscorbutic solution inactivated it. On the other hand, boiling such a solution for two hours in an atmosphere of carbon dioxide caused no marked diminution in the antiscorbutic potency. Ducher, Harshaw and Hall[2] likewise found that the antiscorbutic properties of orange juice are susceptible to oxidization, but in the absence of oxidizing agents are stabile to heat up to the boiling temperature.

It is fairly generally conceded that infants brought up on natural milk do not contract scurvy. Wilkinson[3] states, however, that he has seen one case in which scurvy developed in a purely breast-fed child. The mother had been living largely on pickles, vinegar and bread. The child rapidly recovered following correction of the mother's diet. Two other instances of scurvy occurring in breast-fed infants are reported by Tupas.[4] One was an infant of two months and the other one month old. The administration of lemon juice without any other change in the diet resulted in prompt improvement. Fabor[5] reports a case of infantile scurvy following the use of raw certified milk from birth. Faber suspects that the sodium citrate added to the milk may have been responsible for the destruction of the antiscorbutic vitamin.

Although scurvy is a common condition, Comby[6] points out that general practitioners are apt to overlook it. From an experience of 72 cases, he has found that in 9 out of 10 patients the disease has not been recognized before the child was brought to him. The diagnosis is established by the three following points, which should always be borne in mind in the case of a child who has been ailing for some little time and has been treated by various methods without success: (1) Artificial feeding for six, eight or ten months with sterilized or condensed milk or infant foods. (2) Pains in the bones, manifested by loss of power in the lower limbs and crying when they are moved—a sign invariably present. (3) Ecchymoses in the gums. This sign, which is pathognomonic, is unfortunately not constant. It was absent in 16 out of Comby's 72 cases, or in 22 per cent. Prophylaxis consists in giving a child who has been fed on sterilized or condensed milk for some months a small quantity of orange juice, grape juice, or lemon juice sweetened with sugar, every day. Treatment consists in substituting boiled fresh milk for preserved milk and giving from one to three teaspoonfuls of orange, grape or lemon juice daily.

[1] Lancet, 1921, **200**, 478.
[2] Journal of Biological Chemistry, 1921, **47**, 483.
[3] British Medical Journal, April, 1921, 583.
[4] Philippine Islands Medical Journal, 1921, **1**, 23.
[5] American Journal of Diseases of Children, 1921, **21**, 401.
[6] Bull. et Mem. Soc. Med. des Hôp. de Paris, March 3, 1921.

While scurvy is not uncommon in childhood, it is quite rare among adults. That it may occur in a pronounced way is evident from the following case report by McClelland.[1] The patient, a man aged forty years, came under observation July 29, 1921, complaining of bleeding teeth. He looked ruddy and sunburnt. His breath was offensive, many of the teeth were carious, and blood was oozing out from the swollen and spongy gums. As fast as it was wiped away from the necks of the teeth, it reappeared. Thousands of petechial ecchymoses were to be seen on the limbs and trunk. There were faint systolic murmurs in all the cardiac areas, with a pulse rate of 100, and a normal temperature. There was no albumin in the urine. The patient was seen on August 2, 4, and 6; the bleeding from the gums continued, while he also complained of weakness and headache. On the evening of the 6th, he became unconscious. Deep coma, with stertorous breathing followed, and he died early on the 7th. Late on the 6th, it was noted that the pupils were equal, but the right arm was very flaccid. Patient called vegetables "pig's food," and appears to have lived principally on bacon, bread and tea.

The frequent occurrence of hemorrhage in patients with scurvy led Bedson[2] to study the blood-picture with particular reference to the platelets. In experimentally-produced scurvy in guinea-pigs and monkeys and in one human case, the platelets were found to be normal in number. It is possible that very transient fluctuations in the platelet count occur in scurvy, and that it is during this period of platelet deficiency that the hemorrhages occur. It is hardly conceivable, however, that in making a comparatively large number of platelet observations, such fluctuations should have been completely overlooked. The red cells in some cases showed an increase in number, this condition coinciding with a "prescurvy" or incipient scurvy stage. In the acute stages of the disease, particularly where hemorrhages were numerous, the number of red cells fell to slightly below the normal. No variations in the total and differential leukocyte count were observed.

Pellagra. THE SPECIFIC CAUSE is unknown. The two schools, those who believe in an infectious origin and those who consider food deficiency as the important factor, continue to advance the old arguments which have been reviewed in these columns in past years. MacNeal[3] summarizes our etiologic, clinical, diagnostic and therapeutic knowledge concerning pallagra. It is his opinion that the specific factor is a living organism, an infectious agent derived directly or indirectly from a previous case and that in addition there is a group of non-specific factors which predispose to infection. In this group are malnutrition, either from inadequate food or inability to utilize food in an adequate manner, cachexia of disease, overwork, depressing influence of hot weather, strain of reproduction in women, involution of old age, alcoholism and many other such influences. The specific causative factor probably

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[1] Lancet, 1921, **201**, 608.
[2] British Medical Journal, 1921, **2**, 792.
[3] American Journal of the Medical Sciences, 1921, **161**, 469.

resides in the gastro-intestinal tract, and the absorption of its products from the digestive tract gives rise to the distant manifestations of pellagra.

In the consideration of the food element, MacNeal assigns a secondary or predisposing role to all such food factors which act by disturbing nutrition, whether as a result of deficient diet, unbalanced diet or what not. The living conditions are likewise an indirect factor, influencing the resistance of the individual. Experimental inoculation, according to MacNeal, has failed in every instance up to the present time. The symptomatology of pellagra was dealt with at length in these columns last year. MacNeal's article contains an excellent review of the clinical manifestations of this disease with the four d's, *dermatitis, diarrhea, delirium and death.*

In the TREATMENT OF PELLAGRA it is well to bear in mind that spontaneous recovery is frequent, that the attacks tend to self-limitation and that the indications are principally supportive and symptomatic treatment. Rest, cheerful enviroment, cleanliness and a liberal diet, including milk as the principal element, are emphasized by MacNeal. After recovery from an attack the effort should be made to prevent recurrence by the removal of all debilitating influences. The nutrition and resistance should be maintained at the highest possible level, especially during the spring and early summer of the following year because of the danger of recurrence at that time.

Diabetes. The literature upon diabetes appearing in recent years has been voluminous. McCay[1] has collected the observations on diabetes in India and recalls certain interesting observations to our minds. The prevalence of the disease there is well known. The blood-sugar of the normal Bengali is 0.13 per cent, a higher figure than that obtained here in America. This is explained on the basis of the larger carbohydrate content of the diet. The opinion is expressed that the predisposing cause of glycosuria is a gastroduodenitis leading to a lesion of the pancreas and a disturbance in the internal secretion of that organ. The cause of death in the diabetes met with in India is said to be almost invariably uremia. There is no evidence of active ketosis with hunger and coma. The uremic coma is the result of the functional derangement of the kidneys brought about by the continued passage of large quantities of sugar over a prolonged period. This onset of this type of coma is not necessarily dependent upon a definite pathological lesion of the kidneys. This work is, unfortunately, lacking in complete proof owing to the absence of postmortem records, an insurmountable difficulty in the present social and caste conditions in India. The last paper deals very thoroughly with the treatment of diabetes in India. One is struck with the ease with which a mere restricted dietary removes the glycosuria, even in marked cases. This is partly explained by the fact that diabetes mellitus in India is of a mild type and differs from the severe form which we see, where death is due to true diabetic

[1] Diabetes in India, being a Collection of Reprints from the Indian Journal of Medical Research. By D. McCay, Major I.M.S., Professor of Physiology, Medical College, Calcutta, and Others.

coma. Again, reduction of the carbohydrate in the diet does not lead to ketosis, and diacetic acid is rarely found. As early as 1913, the plan of inducing a raised glucose tolerance by gradually increasing the carbohydrates was adopted. This in essentials was the same plan of treatment as that devised by F. M. Allen and worked out quite independently by McCay. The difference was that starvation, as advocated by Allen, was not ordered, simply because it was quite unnecessary in the treatment of the mild type of case met with in India.

CERTAIN ETIOLOGIC FACTORS. The frequency of *trauma* preceding diabetes has been studied by Diez.[1] He found the following statistics: In 20 out of 225 cases (Griesinger); in 2 per cent out of 4068 cases (Frerichs); in 1.4 per cent out of 938 cases (Seeger); in 5 per cent out of 116 cases (Ebstein); in 1 per cent out of 800 cases (Senator); in 5.6 per cent out of 669 cases (Külz-Rumpf). Cantani found a history of trauma in 10 per cent out of 1004 cases of diabetes, but, as Ferrranini observes, cases were included in which diabetes had occurred fifty years after the trauma. According to Brouardel and Richardière, traumatic diabetes is commoner in men than in women, while Lépine considers that children are most likely to be affected. Diez, however, thinks that these statistics have only a relative value, because the observers had not made an exhaustive inquiry into the etiology. While all writers admit the existence of a traumatic transitory glycosuria, some, like Jaccoud, deny the existence of a true traumatic diabetes, and consider that trauma only rouses preëxisting diabetes into activity. Others believe in the possibility of the development of traumatic diabetes when an hereditary or acquired predisposition is present. The opinion generally held is that of Richardière and Sicard, who maintain that the action of trauma is merely to awaken dormant disease. The region affected by the trauma is important. In 33 cases Brouardel found cranial trauma in 17, spinal trauma in 5, and traumata of other parts of the body in 11. Traumatic diabetes often appears early, sometimes within three days or a week of the injury, but there may be an incubation period of several weeks or as much as sixteen months. If diabetes occurs two years after an injury, it has no relation to the trauma. The onset may be acute and the subsequent course rapid or slow, or it may be insidious and progressive from the first. The symptoms are the same as those of spontaneous diabetes.

Heger[2] records a case which seemed to him to support the view that diabetes may follow injury. A boy, aged fourteen, was knocked down by a car and sustained a fracture of the base of the skull. He was unconscious for four days. Fifteen days later the boy had so much improved that he was sent home. Soon after this he began to waste, developed polyuria, weakness and mental depression. Five weeks after the accident he was passing three and a half liters of urine per diem, containing 139 gms. of sugar. Before the accident, the boy had enjoyed good health. Under appropriate treatment, the glycosuria

[1] Policlinico, 1921, **28**, 431, abstract British Medical Journal, 1921; Epitome, April 23, 66.
[2] Le Scalpel, June 25, 1921.

disappeared in four or five months; at the end of the sixth month, there was no trace of sugar and the boy was in good health.

Diabetes caused by infection of the tonsil with subsequent infection of the pancreas is a view which Blodgett[1] maintains in a report of 4 cases of what he terms the acute pancreatic form. In each instance the clinical history would seem to point to such a possibility.

Diabetes after mumps is reported by Labbe and Debre.[2]

Diabetes, Syphilis and the Negro. We have referred in past years to the views of Warthin, and others, in regard to the syphilitic origin of diabetes. Lemann[3] investigated this subject from a unique viewpoint. The syphilization of the negro is a matter of common knowledge to all practitioners in the South. They present a material enormously rich in every aspect of the disease, because, owing to their ignorance and poverty, they go frequently untreated or inadequately treated. If, therefore, syphilitic pancreatitis is the common cause of diabetes, we should find the diabetes more prevalent among them than among the whites. This, however, is not the case. While this disease is not rare in the negro, still the incidence is not as great among them as among the whites. At the Charity Hospital, New Orleans, among 160,044 admissions there were 135 white diabetics and 59 negro diabetics. The negroes furnished 43 per cent of the admissions, and only 30 per cent of the diabetics. The incidence of diabetes in New Orleans has increased in recent years, the increase occurring fairly equally among whites and negroes. That syphilis is not a factor is evidenced further by the fact that although the negroes form about 40 per cent of the admissions and about 30 per cent of the diabetics, they furnish more than 50 per cent of all the syphilitic disease. The only exception to the rule that the negro furnishes more than his relative share of any syphilitic disease is locomotor ataxia. It would appear, therefore, that we must accept one of two explanations of the smaller incidence of diabetes among the negroes and its possible relation to the theory of syphilitic pancreatitis as a common cause of diabetes mellitus. First, that there is no relation between the incidence of diabetes and syphilis; hence there is no probable etiologic relation between the two. Or, secondly, that there is an unexplained immunity of the negro race to the production of spirochetal pancreatitis just as there is an unexplained immunity of the race to the production of locomotor ataxia. Lemann is convinced of the validity of the former for reasons given above.

Glycosuria of Malarial Origin is reported by Castellani and Willmore[4] and Harrison.[5] The former record 2 cases in which malaria was apparently a definite etiologic factor, since both cases were cured by the administration of quinine in full doses without any dietetic treatment. Harrison reports in detail the case history of his patient, who likewise

[1] Pennsylvania Medical Journal, 1921, **24**, 407.
[2] Bulletins de la Societe Medicale des Hôpitaux, Pons, July 29, 1921.
[3] American Journal of the Medical Sciences, 1921, **162**, 226.
[4] British Medical Journal, August 20, 1921, 286.
[5] Ibid., October 22, 1921, 630.

cleared up with quinine in the absence of dietetic treatment; in fact, sugar was deliberately included in the diet throughout the hospital stay. Harrison suggests that the diagnosis of "glycosuria of malarial origin" is preferred to that of "mild diabetes in a malarial subject."

Sapremic Glycosuria is reported by Higginson[1] in a patient who had a carbuncle on the back of his neck and then discovered he had gylcosuria. Contrary to the usual belief, the carbuncle was the cause of the glycosuria and not *vice versa;* in other words, it was a case of sapremic glycosuria. In sapremic glycosuria the sugar is relatively small in quantity. The largest quantity recorded by Higginson as having been passed in twenty-four hours is 1400 grains (or 3 ounces). In diabetes, the patient commonly passes from one-half to three-quarters of a pound, say, from 4000 to 6000 grains daily. Consequently, in sapremic glycosuria there is an absence of those distressing diabetic symptoms, hunger, thirst polyuria and emaciation. Mitchell[2] reports a similar experience. In discussing sapremic glycosuria, Cammidge[3] expresses the opinion that lowered carbohydrate tolerance is the primary condition. His chief reason for saying this is the finding of high blood-sugar values in all cases of furunculosis including those without glycosuria. In those instances in which glycosuria appears and then disappears after removal of the septic focus, it must be borne in mind that, just as a high blood-sugar does not necessarily result in glycosuria, so the disappearance of sugar from the urine may be due to other causes than improved carbohydrate metabolism. His experience has been that glycuronic acid, pseudolevulose, and more rarely true levulose and pentose, either alone or with dextrose, occur more commonly in toxic conditions than pure dextrosuria. The pseudoglycosurias are no doubt part of a protective mechanism, and probably arise from defects in the functions of the liver consequent on the toxemia, so that one would expect them to clear up when the source of the toxin is removed. A true dextrosuria is a different matter, and although some improvement in tolerance may take place so that sugar is only present in the urine intermittently, and when carefully looked for by delicate tests, complete cure does not occur, and examination of the blood will often show a high sugar content.

Some factors controlling the normal sugar content of the blood is the subject of a report by Cammidge, Forsyth and Howard.[4] The summary of their findings is as follows: (1) The liver contains a diastatic ferment, the action of which is reversible. (2) In the fasting state the glycogenolytic activities of this ferment are very largely inhibited by: (*a*) an antiferment formed by the pancreas; (*b*) the impermeability of the resting liver cells to sodium chloride; (*c*) the reaction of the fasting blood and liver cells. (3) As long as the pancreas and liver are functionally intact and a flow of blood with a normal reaction is maintained, glycogenolysis will be constant therefore and the sugar content of the blood vary within very narrow limits. This is true of all animals of similar constitution, no matter what their habitual

[1] British Medical Journal, 1921, **1**, 296.　　　[2] Ibid., **1**, 459.
[3] Ibid., **1**, 511.　　　[4] Ibid., **2**, 586.

diet may be. (4) The entrance of food into the stomach causes a flow of acid, and when this acid reaches the duodenum a formation of secretin results. (5) The secretin (*a*) stimulates the liver cells to produce bile, thus permitting the entrance of sodium chloride, which activates the diastatic ferment; (*b*) causes the pancreas to pour out its alkaline secretin into the intestine to combine with the acid gastric contents, forming acid salts and sodium chloride, which pass to the liver and increase the activity of the diastatic ferment; (*c*) interferes with the formation of the internal secretion of the pancreas, thus diminishing its inhibitory effect on glycogenolysis in the liver. (6) Carbohydrates reaching the liver from the intestine or formed from proteins in the liver are converted into glycogen by the diastatic ferment, the efficiency of the process depending upon the extent to which the glycogenolytic action of the enzyme is inhibited by the internal secretion of the pancreas. Unless the power of glycogen formation possessed by the liver is exceeded, sugar as such, or formed from starch in the intestine, does not pass into general circulation or play any direct part in the rise of blood sugar following feeding. This theory appears to account for the constant level of the normal sugar content of the blood in a fasting condition and to explain the variations produced by the ingestion of food. It also permits of a reasonable explanation of the changes occurring in disease. There are no doubt other factors, such as emotional excitement, nervous disturbances, changes of temperature, etc., which affect the percentage of sugar in the blood, but these are probably of comparatively minor importance under normal conditions.

Glycemia and Glycosuria. Fitz and Bock[1] studied the total amount of circulating sugar in the blood in normal persons and in diabetics. In the normals the total amount varied, but did not exceed 7.5 gm. The plasma sugar was almost always considerably greater than the corpuscular sugar, but it did not exceed 4.85 gm. The total amount of sugar in the blood of 9 diabetic patients also varied considerably. The highest blood-sugar content estimated was 15 gm., and the highest plasma sugar was 10.78 gm. The plasma of the diabetic bloods, relatively, contained much more sugar than did the corpuscles. This suggests that the plasma in diabetes is a vehicle for the transportation of sugar from the body cells, which are unable to burn or store it, to the kidney which excretes it. The corpuscular sugar tends to be fixed within rough limits, though increased in polycythemia and decreased in anemia. Glycosuria does not occur unless the plasma sugar exceeds a certain threshold. Blood-sugar concentration expressed as milligrams per hundred cubic centimeters of blood or plasma may give misleading information with regard to the total amount of circulating sugar. The threshold at which glucose appeared in the urine of the diabetic patients of this series seemed to lie between 5.20 and 5.36 gm. of total plasma sugar. According to Fits and Bock, the total plasma sugar offers a more rational basis of comparison with sugar excretion than does the plasma sugar concentration alone.

[1] Journal of Biological Chemistry, 1921, **48**, 373.

The variation of the blood-sugar tolerance with age is maintained by Spence.[1] Of 5 men over sixty years of age, 4 showed a marked diminution of carbohydrate tolerance with consequent hyperglycemia. In children under three years of age, a low blood-sugar curve must be taken as the expression of the normal sugar tolerance; in children above that age, the blood-sugar curve resembles that of a young adult. In cases of cancer, the sugar tolerance was variable. It was normal in the younger and decreased in the older patients. This suggested that the hyperglycemia and decreased sugar tolerance, which have been described in some cases of nephritis and in cancer, are due to the hyperglycemia of old age, which is so frequently present even in apparently healthy old people. In this connection, although not particularly germane in this review, one recalls the recently reported work of Friedenwald and Grove[2] who claim that the blood-sugar tolerance test is of great value in differentiating malignant and benign diseases of the gastro-intestinal tract, especially in obscure cases, when taken into consideration with the other clinical evidence. It is important that diabetes, nephritis, tuberculosis and disturbances of the thyroid should always be excluded before the tolerance test is undertaken, inasmuch as hyperglycemia is frequently present in these affections. This test has proved positive in 72 of the 75 cases of cancer of the gastro-intestinal tract and Friedenwald and Grove state that there can be but little question of its value as a diagnostic measure, even though it was found positive in 5 cases of non-malignant disease of these organs.

Glycemia and glycosuria are discussed in detail in the three Goulstonian Lectures which were given in the past year by Graham.[3] To the reader who wishes to refresh his memory on the fate of the sugar in the blood in normal and abnormal conditions and with regard to the conditions under which sugar is excreted in the urine, and especially with regard to the causation and treatment of diabetes, the Goulstonian Lectures contain a wealth of information.

CLINICAL NOTES ON DIABETES. The *significance of diabetes mellitus in mental disorders* is discussed by Pike[4] in a report of 3 cases. In 2 instances the glycosuria occurred as an independent affection in patients suffering from mental disease. The development of diabetes was without influence on the type or degree of psychic manifestation. In the third patient the diabetes was the etiologic factor in the development of the psychosis. Under treatment for the diabetes, the mental symptoms disappeared, to return with the failure to follow the treatment. This patient represents a group which begins with evidences of a mild depression, gradually develop ideas of poverty and of sinfulness, to which are frequently added delusions of persecution; and when they become aware of the underlying physical condition, hypochondriacal ideas with reference to the excretion of sugar are added and often dominate the psychic manifestations. In these cases, improvement of the

[1] Quarterly Journal of Medicine, 1921, **14**, 314.
[2] American Journal of the Medical Sciences, 1922, **163**, 33.
[3] Lancet, 1921, **200**, 951, 1003 and 1059.
[4] Journal of the American Medical Association, 1921, **76**, 157.

sugar metabolism is marked by a corresponding approach to normal mental functioning.

Kahn[1] calls attention to the *angina pectoris of diabetes*. He states that among diabetics, a man of middle age or a woman nearing her menopause or during her climacteric will frequently complain of the distressing pain in the region of the heart. Although uncomplicated diabetes is associated with a low blood-pressure, and the presence of renal changes is associated with a high blood-pressure, attacks of angina pectoris may be found among the former. The pain may not be very excruciating but still induces marked anxiety. Often the pain radiates to the neck or left shoulder and arm. These anginal attacks do not seem to occur when the patient's glucose tolerance is not exceeded. Electrocardiographic studies of a number of the diabetic patients show an inversion of the T-wave in one or more of the three leads, which Willus recently has pointed out, is usually due to some myocardial pathologic condition.

Blood-pressure studies in diabetes were made by Hitzenberger[2] who found in 97 diabetics and 561 non-diabetic controls the blood-pressure was above normal in the elderly and below normal in the younger diabetics, compared with the average for their age.

When *hirsutism occurs in diabetes*, as reported by Weil and Plichet,[3] it is not a mere coincidence. It usually indicates a polyglandular endocrine disturbance in which pancreas, ovary and adrenal are involved. This form of diabetes, whether slight, moderate or severe, is similar to that found in other diseases of the endocrine glands, such as acromegaly of Graves's disease, in which involvement of the hypophysis or thyroid affects the hepatico-pancreatic system, which controls the metabolism starch.

The occurrence of *retinitis in diabetes* seems to be dependent more upon the accompanying pathologic changes in the vascular system than upon the active metabolic disturbances which occur as a result of the diabetes. Wagener and Wilder[4] state that retinitis characteristic or diagnostic of diabetes, comparable with the retinitis of nephritis, must still be regarded as unproved, and retinitis in uncomplicated cases of acute diabetes, diabetes gravis, does not occur. It was not present in 80 consecutive cases of this severe type of the disease in a group of 300 diabetics. Cases of diabetes with retinitis are always or almost always complicated by vascular or renal disease, and the diabetes tends to be mild and chronic. This was true in all of the 23 consecutive cases of this kind found in the study of the 300 patients.

Edema occurring *in diabetics* is usually of serious moment. Wilder and Beeler[5] call attention to its occurrence in cachetic patients without evidence of cardiac or renal disease. It occurs with a lowered threshold for chlorides when nephritis is not a complicating factor. Both the edema and the behavior of the chloride threshold are inde-

[1] Journal of the American Medical Association, 1921, **76**, 570.
[2] Wiener Archiv. für innere Medizin, 1921, **2**, 461.
[3] Bull. et Mém. Soc. Méd. des Hôp. de Paris, March 10, 1921.
[4] Journal of the American Medical Association, 1921, **76**, 515.
[5] American Journal of Physiology, 1921, **55**, 287.

pendent of the state of the acid-base equilibrium of the body, as measured
either by the carbon dioxide capacity of the plasma or by the titratable
acid or ammonia excretion of the urine.   Increasing edema and lower-
ing chloride threshold may accompany diminishing acidosis, and *vice
versa*.   They are likewise independent of the degree of glycemia and
of the presence or absence of glycosuria.   Hence, Wilder and Beeler
conclude that edema in diabetes differs fundamentally from the edemas
in diseases of the heart and kidneys.   The determining factor seems
to be inanition, which relates it to the hunger edema of war times
and other edematous conditions of undernutrition.

TREATMENT OF DIABETES.   The objects of the diet adjustment in
diabetes and the methods of Joslin and Allen are fairly generally under-
stood, and yet the literature on the subject, to quote Woodyatt,[1] is still
confused by lack of unanimity among all writers as to the best manner
of handling all cases.

Newburgh and Marsh,[2] failing to achieve practical results by their
application of the principles of "total dietary restriction" and "under-
nutrition," resort to low-protein high-fat diets with striking success
in the management of 74 cases.   Woodyatt refers to the "milk cure,"
"rice cure," "potato cure," "oatmeal cure," and states that his study
was made in the effort to correlate some of the varying views of
different writers.   He maintains, that it is necessary to understand
the nature of the diabetic anomaly which is characterized by an in-
ability on the part of the body to utilize as much glucose as may be
utilized by the normal body when the supply of glucose exceeds certain
limits.   This limitation is the characteristic of diabetes.   The pancreas
has to do solely with the disposition of glucose and that to lessen its
work in order that it may recuperate, one must lessen the quantity
of glucose entering the metabolism.   Abnormal ketogenesis is not due
directly to any impairment of the endocrine function of the pancreas.
It is a secondary effect due to the withdrawal of the oxidizing (dis-
sociated) glucose.

There is a definite ratio between the quantity of glucose oxidizing in
the body and the maximum quantity of ketogenic fatty acids that can
be oxidized in the same time without the appearance of abnormal
amounts of the acetone bodies.   In other words, the quantity of oxidiz-
ing glucose fixes an upper limit to the quantity of ketogenic fatty acid
that can be completely oxidized at the same time.   Shaffer[3] and Wood-
yatt state that for the present it is safe to assume that the ratio of higher
fatty acids to glucose in the proportion of 1.5 to 1 (in gm.) will lead to
acidosis if exceeded.   Woodyatt states, therefore, that the rationale
of dietetic management in diabetes is to bring the quantity of glucose
entering the metabolism from all sources below the quantity that can
be utilized without abnormal waste; and to adjust the supply of fatty
acids in relationship to the quantity of glucose so that in the mixture
of foodstuffs oxidizing in the body the ratio of the ketogenic fatty

[1] Archives of Internal Medicine, 1921, **28**, 125.
[2] Ibid., 1920, **25**, 647.
[3] Journal of Biological Chemistry, 1921, **46**, 98.

acids to glucose shall not exceed limits compatible with freedom from ketonuria. Woodyatt states that if the ingestion of fat spares the tissue fat and thus prevents the protein loss from becoming abnormally great, and if the quantity of fat metabolized is the same whether coming from the tissues or from the diet, then one is justified if these premises are sound in asking why should we ever use complete fasting for diabetes?

To quote Woodyatt further: Granting that a diabetic patient may suffer from obesity as well as diabetes—that he may have two different metabolic defects; or granting that at times it might seem desirable to starve for other conditions besides diabetes: In such cases fasting would be rational, if it would improve the general condition. But for diabetes itself, and particularly for diabetes associated with undernutrition, why for the purpose of desugarization should the patient be compelled to draw from his tissues the fat that he might draw from a diet, especially if, in drawing from his tissues, he lowers his fat reserves to the extent that he increases his protein losses?

All the foods introduced into the body except a small fraction of the protein resolve themselves into two things: glucose on the one hand, and higher fatty acid (or ketone equivalents) on the other. Woodyatt puts it this way:

100 gm. carbohydrate yields in the body	100 gm. G and	0 gm. FA
100 gm. protein yields in the body . .	58 gm. G and	46 gm. (?) FA
100 gm. fat yields in the body . . .	10 gm. G and	90 gm. FA

These relationships may be expressed in the form of simple equations in which G is the total quantity of glucose introduced into the body by a given food combination; F A the total quantity of higher fatty acids (plus ketogenic amino-acids expressed in terms of higher fatty acid); C, carbohydrate; P, protein; and F, fat (neutral); thus:

$$(1) \quad G = C + 0.58\,P + 0.1\,F$$
$$(2) \quad F\,A = 0.46\,P + 0.9\,F$$

If the ratio of F A : G which if exceeded leads to acetonuria is 1.5 : 1, then when $\frac{F\,A}{G} = 1.5$ we derive from (1) and (2) the equation $F = 2C + .54\,P$, which for clinical purposes may be stated simply as

$$(3) \quad F = 2C + \frac{P}{2}$$

In the estimation of optimal diets, one must remember that the ratio $\frac{F\,A}{G}$ must not exceed 1.5; glucose is contained not only in the carbohydrate, but also approximately in one-half of the protein and one-tenth of the fat; the fats are desirable because of their calory value, but are dangerous in their high fatty acid content; the protein requirement estimated conservatively is 1 gm. per kg. body weight. In a hypothetical patient weighing 50 kg. and able to utilize 100 gm. of glucose, Woodyatt

figures out the diet as follows: Thus, if 100 gm. is the highest quantity of glucose derived from all sources that the patient can utilize, 100 gm. $= C + 0.58\ P + 0.1\ F$. In order to secure the maximal number of calories, the diet must clearly contain every possible gram of fat (at 9 calories per gram) that the value of G and the relations expressed in the formulas 1 and 3 given above, will permit, and consequently the lowest possible carbohydrate protein fraction (at 4 calories per gm). Also, as between carbohydrate and protein, the protein must be as low as possible and the carbohydrate as high as possible, for 1 gm. carbohydrate yielding 1 gm. glucose and 4 calories provides for the normal oxidation of 1.5 gm. of higher fatty acid. On the other hand, 1 gm. protein having the same caloric value as carbohydrate yields less glucose to support fat combustion and besides this yields acetone itself. If the body weight of the patient be 50 kg. and 1 gm. protein per kg. is selected as a conservative minimum; then P becomes 50 gm. and the equation (3),

$F = 2C + \dfrac{P}{2}$ becomes $F = 2C + 25$. We have already made $G = 100$ gm.

Now, the glucose yielded by the 50 gm. protein will be 0.58×50, or 29 gm., leaving $100 - 29$, or 71 gm., to be distributed between carbohydrate and fat. In other words, $C + 0.1F = 71$. From this we obtain $F = 710 - 10C$. But we also have from the above, $F = 2C + 25$. So $2C + 25 = 710 - 10C$, solving which $C = 57$ gm. (57.08). Substituting this value for C in $F = 2C + 25$ we find $F = 139$ gm. (139.16). Then the optimal food combination that will fulfil the conditions and relations specified is: Carbohydrate, 57 gm.; protein, 50 gm.; fat 139 gm.; calories, 1680. Proving this diet, we find the total glucose equivalent $G = 57.08 + (0.58 \times 50) + (0.1 \times 139.1) = 99.99$ as called for. Also $F\,A = (0.46 \times 50) + (0.9 \times 139.1) = 148.19$ and $\dfrac{F\,A}{G} = 1.5$ as required.

It is apparent, that any addition of any foodstuff to this diet will make G greater then 100. If, on the other hand, one added more fat—say, 10 gm. and subtracted 1 gm. carbohydrate, G would remain 100 and the calories would be increased by 86, but this would make $\dfrac{F\,A}{G}$ greater than 1.5.

The space of this review will not allow of a detailed comment on the interesting case report in Woodyatt's paper, to which the reader is referred. Briefly, an acutely ill patient with very severe diabetes could be made to utilize all the glucose of which he was capable, provided that his food supply was properly adjusted. On low diets, glycosuria was present even though the glucose was below the utilization point. On these low diets which failed to meet maintenance requirements the patient was thrown back on his own tissues for food. If the patient had been fat, Woodyatt points out, following Lusk, much fat would have burned but little protein. In this patient, however, there was very little fat and much of the protein apparently was burned. This patient then, on fasting, was equivalent to being on a pure protein ration. When this patient was placed upon fat in the form of a rice-butter diet, the excess of protein breakdown was stopped

with the associated glucose formation from the breaking up of the protein molecule. In other words, this patient in fasting and on a low diet catabolized so much protein that his protein sugar overtaxed his tolerance limit, so that when a diet sufficient to maintenance was instituted, resulted in a disappearance of the glycosuria by preventing the endogenous factors of food supply from coming into action.

The retention of protein during the diet reduction is advocated by Fenlon.[1] The procedure is essentially the maintenance of the protein intake at a moderate level, the restriction of the fat and the relatively rapid reduction of the carbohydrate until the patient's glycosuria disappears. The carbohydrate tolerance is then built up by a gradual increase in the carbohydrate intake. Forty cases have been traced under this method. The mortality was 5 per cent (2 cases). With the exception of 1 case, which showed a slight amount of acetone, all cases were sugar- and ketone-free upon discharge. This method has been found applicable to patients of all ages.

Newburgh and Marsh[2] report their studies of the use of high fat diet in the treatment of diabetes mellitus. Their observations are made on 73 cases of true diabetes mellitus, the majority of which were of the severest type. Despite this fact, they had succeeded in rendering and keeping their patients sugar-free up to the time of discharge from the hospital.

The authors summarize their observations as follows: Patients with severe diabetes, as a class, do not remain sugar-free on the usual high protein diet unless the total energy intake is kept so low that incapacity from starvation results. The only satisfactory diet is one which will keep the diabetic sugar-free, which will prevent the occurrence of serious acidosis, which will maintain nitrogen balance and which will make it possible for him to resume the ordinary activities of life. The high fat, low protein, low carbohydrate diet is capable of fulfilling these four specifications. The blood-sugar determination in 45 cases treated by this method showed a reduction to within normal limits in all but 4. Of the 5 which did not reach a desirably low percentage, 2 were suffering from severe complicating diseases and one was suspected of not adhering to the diet.

The experimental studies of Allen[3] show that the assimilative power of diabetic animals rises and falls inversely with the body weight. This principle is important clinically in that undernutrition should be continued to the point of relieving the pancreatic function from overstrain revealed by the most delicate tests, particularly hyperglycemia. With extremely few exceptions in human patients, the curve of rising tolerance intersects the curve of falling weight at some level on which life can be maintained. Lack of thoroughness in relieving the pancreatic function is the chief cause of continued deterioration of this function, and the consequent choice between coma and starvation.

[1] American Journal of the Medical Sciences, 1921, **161**, 193.
[2] Archives of Internal Medicine, 1920, **26**, 647, and 1921, **27**, 699.
[3] American Journal of the Medical Sciences, 1921, **161**, 16.

With regard to the effects of exercise, Allen and Wishart[1] conclude from their experimental studies that the increased metabolism of exercise does not impose an added strain upon the internal pancreatic function. For purposes of practical treatment, the combustion of food by exercise is preferable to its deposit in the body, but exercise cannot replace dietary restriction or permanently atone for excessive diets. The fundamental value of exercise is probably as a form of undernutrition. Heavy exercise involves undesirable fatigue and strain, but light exercise aids health. Rest is necessary in the severest cases.

The Allen method of treatment has been in use approximately five years. That it represents today a distinct advance over our older methods, is evidenced by fairly general experience. One of the latest evaluations of the method is that of Williams[2] who states with regard to influence on life expectancy, that in young people, in whom the disease is most serious, it would appear that it is at least doubled. Middle-aged and elderly diabetics who are not too seriously afflicted with complications and when faithful to the treatment can probably survive the life-expectancy of the average normal individual. The Allen method is of the greatest service when instituted early in the disease. Like tuberculosis and cancer, diabetes should be recognized and thoroughly treated in its incipiency. Most of the failures in its use are due either to serious complicating disease, or more frequently to unfaithfulness on the part of the patient.

That the "diabetic must not expect a varied diet" is controverted by Orton.[3] He gives a long list of vegetables for use which are ordinarily not found in the markets. For the diabetic who can have his own garden, the raising of many kinds of vegetables affords a useful hobby. Orton gives the directions for the preparation of vegetable soups, cooking vegetables in an appetizing way and for the making of tasty salads. He tells of the canning and marking of vegetables with the percentage F C and P and caloric values so that the diabetic can carry his meals with him. There is a need for a supply of those varied vegetables when the diabetic cannot grow them in his own garden. Orton's paper makes interesting reading to one interested in diabetic diets.

With regard to *foci of infection*, Fenlon[4] states that diseased teeth, tonsils, etc., are removed during the patient's stay in the hospital, the diet being established before operation. Lyon and Meakins,[5] after discussing the diabetic measures at length, state that septic foci should be sought for and removed, since a gumboil or carious tooth may account for the persistence of a glycosuria. Although the use of saccharin is widely practiced, Grundfest[6] reports an example of idosyncrasy to it. The case was that of a man, aged forty-five years, who three days after taking saccharin for the first time to sweeten his coffee, presented a bloated face, swollen eyelids and chemosis, together with a feeling of irritation in the larynx. On discontinuing the saccharin, the symptoms rapidly

[1] American Journal of the Medical Sciences, 1921, **161**, 165.   [2] Ibid., **162**, 62.
[3] Ibid., **162**, 498.   [4] Ibid.
[5] Edinburgh Medical Journal, November, 1921.
[6] Zentralbl. f. inn. Med., March 26, 1921.

disappeared. When the use of saccharin was resumed some days later the symptoms returned, and Grundfest considered an idiosyncrasy to exist.

THE PREVENTION OF DIABETES. In last year's PROGRESSIVE MEDICINE we reviewed at length Joslin's article dealing with the prevention of diabetes. It will be recalled that he believes diabetes is largely the penalty of obesity, the excess of fat implying too much food or too little exercise, or both combined. The measures of prevention, therefore, are obvious. The actual detection of incipient or latent diabetes would seem necessary in the next step toward reducing the morbidity and mortality of this disease. Sherrill,[1] using the blood-sugar tolerance determinations, found that when there is distinctly abnormal hyperglycemia after mixed meals, and when the ingestion of 100 gm. of glucose produces an elevation of blood-sugar which exceeds the normal in both height and duration, a definite diagnosis of diabetes is afforded. His conclusion is based on the number of positive tests of this character in families having diabetic members, the insensible gradations by which the slighter degrees of impaired assimilation are merged with the cases of alimentary glycosuria and of frank diabetes, and the existence of mild diabetic symptoms in a high proportion of the cases which react positively, which clear up under antidiabetic diet and under no other treatment. Caution in the interpretation of the blood-sugar curve is necessary, however, in view of similar findings in thyroid disturbances, cancer, various toxic states, etc. When, however, these conditions can be excluded in an individual who shows a blood-sugar curve of increased height and duration, potential, latent or incipient diabetes should be considered. As Sherrill states, there is an enormous number of latent or incipient diabetics, with or without symptoms, which have heretofore escaped diagnosis. Our greatest service to these patients may be looked for in the earliest possible diagnosis and prophylaxis, before serious symptoms have ever occurred or severe dietary privations have become necessary. Joslin[2] tells us the encouraging news that in the past year statistics reveal a decline in the mortality from diabetes in the United States. He cautions against too much reliance on the blood-sugar tolerance test. He affirms the reliability of the age, height, weight relationship which was referred to in the preceding paragraph of this review. He also refers to the relationship of gall stones. There were 22 cases of gall stones among his first 1100 cases. The next 1100 cases of diabetes showed 30 cases of gall stones, possibly because more interest was taken in the discovery of this condition. As few individuals under thirty are liable to gall stones, the proportion of gall stones in this series is much higher than 2 per cent; indeed it rises to 4 per cent or a little more. Presumably, a later series will show a still higher percentage. One other factor in the study of gall stones and diabetes was the time of onset of the symptoms of gall stones and of the diabetes. The gall stones began at forty-three years in each series, but the onset of the diabetes was at forty-nine years in

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[1] Journal of the American Medical Association, 1921, **77**, 1779.
[2] Ibid., 1784.

the first series and at forty-five years in the second, possibly again showing closer attention being paid to the connection of diabetes to gall stones in the taking of histories. Hence, in the prevention of diabetes, one should bear in mind the desirability of removing gall stones when symptoms therefrom develop, or even before.

Renal Glycosuria. The diagnosis of renal glycosuria depends on: (1) Glycosuria without hyperglycemia; (2) little, if any, relationship between the amount of sugar excreted and the amount of carbohydrate ingested, and (3) the absence of diabetic symptoms. To these Strouse[1] adds: (4) That the patient must not subsequently develop diabetes mellitus, or show a disturbance of carbohydrate metabolism similar to that found in diabetes mellitus.

Marsh[2] reports an interesting patient who, during a period of four months, excreted an average of 60 gm. glucose daily with a variation of from 15 to 122 gm. The amount was not related to the carbohydrate intake. After the ingestion of 100 gm. glucose, the blood-sugar rose from a fasting per cent of 0.071 to 0.092 in thirty minutes; by the end of two hours it had fallen to 0.043 per cent, and after five hours it was found to be 0.068 per cent. Even with a blood-sugar as low as 0.043 per cent, glucose was excreted at the rate of over 5 grams per hour. Diuresis by increased water ingestion caused no increase in the glycosuria, and no effect was seen from the administration of diuretin in large doses. No evidence of nephritis was found. The D : N ratio in the urine of starvation was about 10 : 1. She reacted to a laparatomy for acute intestinal obstruction in a perfectly normal manner.

Hemochromatosis. In a discussion on this subject before the British Medical Association. Dunn[3] pointed out that the term hemochromatosis has come to be applied to that peculiar morbid condition in which there is an accumulation of free iron-containing pigment in certain parenchymatous organs and in the skin, associated with hepatic and pancreatic fibrosis, with glycosuria in some cases. In a well-developed case there is an obvious rusty color of the liver, pancreas, and retroperitoneal glands. These organs give an intense Prussian blue reaction. In other organs not obviously pigmented, the iron reaction may likewise be obtained. Histologic studies reveal pigmentation in proportion, more or less, to the strength of the iron reaction applied macroscopically. Dunn also points out that in the liver intracellular reaction is more intense than that of the pigment in the interstitial tissues, which suggests that the intracellular iron is chemically in a more free condition. In the pancreas, the islands of Langerhans are less pigmented than the ordinary gland tissue. The spleen reacts intensely; the heart, lungs, stomach, and thyroid may show a fairly deep coloration; the kidneys usually react rather faintly, as do the intestines and skin. The peripheral lymphatic glands in the neck, axillæ and groins usually show little, or no, coloration. In cases in which the bone marrow is examined, it is usually observed that there is no hyperplasia

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[1] Archives of Internal Medicine, 1920, **26**, 768.   [2] Ibid., 1921, **28**, 54.
[3] Section of Pathology and Bacteriology, Lancet, 1921, **201**, 334, and British Medical Journal, November 12, 1921, 783.

of red marrow, the condition being in marked contrast to that observed in pernicious anemia and other hemolytic conditions in which free iron is deposited in the viscera. It would seem that, apart from the liver and pancreas, the hemosiderin granules are not associated with special degenerative phenomena in the tissues.

The above description applies to the terminal stages of the disease where death results from the hepatic changes or from the diabetes incident to pancreatic disturbance. It is well known, however, that well-marked lesions due to pigmentary changes may be absent in the presence of glycosuria, but earlier stages are frequently unassociated in any symptoms and especially with glycosuria. Dunn reports briefly the postmortem findings of three early cases in which death occurred from other causes. In each the liver showed fairly abundant pigment deposit with a very slight cirrhosis. The pancreas in one showed an abundant intracellular pigmentation except in the islets of Langerhans with slight interstitial changes. In the second the only abnormality was a slight cirrhosis with pigmentation in the glandular acini in the neighborhood of the islets. In the third case the cirrhosis was more marked, but no pigmentation either in acini or in islets. From a review of these three cases, it would seem that neither pigmentation nor cirrhosis is a causative of the other, and presumably the second was due to some third unrecognized cause.

Dunn goes on to discuss the *chemical analysis of the organs* in hemochromatosis and states that in this way estimations have elicited important facts regarding the probable duration of the morbid process. In the normal body, the total amount of iron is about 5 gms., of which roughly one-half is in the hemoglobin of the blood. All of the tissues contain a minute percentage, the liver and spleen containing the most. The iron balance is fairly well maintained on the ordinary dietary of about 10 mg. daily. In advanced cases of hemochromatosis there is no evidence of alteration in the total amount of iron in the blood, while the excess in the organs is very great. It is not exceptional for the iron in the liver to amount to 7 per cent of the dried substance of the organ, that is about 100 times the normal percentage, and for the total amount of iron in the liver to exceed 30 gms. There is also an increase of the iron present in the other organs. If, however, we consider the liver alone, and estimate the iron in the diet as 30 mg. per day—a figure well in excess of the known analyses—then it would take one thousand days for the accumulation of the 30 gms. in the liver, assuming that all the iron in the food was absorbed and none excreted. In point of fact, retention of iron was not always absolute. None had been discovered in the urine by different observers, but a certain amount, though less than normal, was excreted in the feces. This meant that the period of development of hemochromatosis must be more than three years, and the iron accumulation was in all probability going on during the whole life of the patient. The excess of the iron was not due to an excessive breakdown of red cells; probably the condition was the outcome of a congenital metabolic peculiarity.

Telling,[1] in continuing the discussion initiated by Dunn, expressed the belief that many cases have probably escaped recognition owing to the disease being relatively unknown, as well as rare. In early cases, though by strict comparison with the normal a certain degree of skin pigmentation might be detected, it may not be of a degree sufficient to lead to a diagnosis during life. Yet he has seen two cases which had already developed—and died from—primary malignant disease of the liver without definite skin pigmentation. The recorded cases are almost all of the advanced type, with characteristic pigmentation and frequent glycosuria; by placing early cases on record, particularly with the striking eventuation in malignant disease, more general attention will be directed to the disease, which will then probably be found to be less rare. It would seem that every case of cirrhosis of the liver, and most certainly every case leading to primary carcinoma, should be carefully investigated from the hemochromatosis point of view. By this means much light will undoubtedly be thrown on pigment metabolism and will enable a final decision to be arrived at as to whether hemochromatosis is a separate morbid entity.

Mackenzie Wallis[2] called attention to the fact that the names hemosiderin and hemofuscin, introduced subsequently by Recklinghausen for the iron-containing and iron-free pigments, should be dropped from usage, since, in the light of our present knowledge, it is possible to show that both pigments contain iron, though in different amounts. The terms were further unsatisfactory in that they implied an origin from hemoglobin, and up to the present time the evidence is against such a supposition.

Cruickshank[3] thought it was useful to make a distinction between the forms of iron found in the tissues. He believes the terms hemofuscin and hemosiderin are of some value. Iron is not present in the same form in every situation. With this opinion Beattie[4] agreed, and, in addition, called attention to the case previously reported by him in which the glycosuria was, as far as he could determine, present for about three years before the bronzing of the skin was noted. Stewart[5] said that he had seen 6 cases of hemochromatosis, postmortem, in the past seven years, and agreed with speakers who expressed the view that the disease was probably more common than was generally supposed. In 2 of the 4 cases, primary carcinoma of the liver coexisted. Bronzing and glycosuria, being late manifestations, were of little use in the early diagnosis of cases, and the presence of hemosiderin granules in the urine, noted by American observers, would probably be found liable to the same defect, since renal siderosis also occurs late in the disease. Inasmuch as the lymph glands, in relation to the liver and pancreas, were among the chief and earliest seats of pigmentary deposition, surgeons ought to examine these glands in cases where, for any reason, the upper abdomen was explored. In the event of brown glands being discovered, one of them might possibly be excised for histological investigation.

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[1] Section of Pathology and Bacteriology, Lancet, 1921, **201**, 334, and British Medical Journal, November 12, 1921, 783.
[2] Ibid.   [3] Ibid.   [4] Ibid.   [5] Ibid.

Blanton and Healy[1] comment on the rarity of this disease, which seems to affect men during middle life almost exclusively. Abbott, in 1901, reported one authentic case in a woman. Four cases are reported by Blanton and Healy, and, in commenting upon the skin pigmentation which may easily be confused with other forms of pigmentation, they state that the only certain method of diagnosis is the microscopic demonstration of iron-reacting pigment in the skin. They believe that there is some toxic agent at work which simultaneously produced injury to the red cells and the parenchymal cells, and causes more circulating iron and a greater accumulation in the injured parenchymal cells. With regard to the associated diabetes, Blanton and Healy believe that it is probably dependent upon changes outside of the pancreas, since the lesions of the islands of Langerhans found in diabetes are so rare in hemochromatosis. These writers state that 81 cases of hemochromatosis have been reported in the literature, of which 75 were available for their study. The liver was reported as enlarged clinically in most instances, markedly in 4 per cent, moderately in 10 per cent, slightly in 60 per cent and no enlargement in 20 per cent. At necropsy, 95 per cent were recorded as enlarged. Ascites occurred in 18 cases. Glycosuria was present in 85 per cent of the cases with a record of such a study (average sugar content 5 per cent). The spleen was more often not enlarged than otherwise on clinical examination. Among 48 cases, 15 had slightly, 2 moderately, and 2 considerably enlarged spleens; 29 were not palpable. The abdominal lymph glands as a rule show massive collections of iron pigment, giving a gross appearance varying from brown to a chocolate color and usually firm. The skin pigmentation occurs in about half of the cases and microscopic studies of the skin show a wide disparity between the striking clinical appearance and the postmortem findings.

Blanton and Healy go on to discuss the frequency of changes in the other organs and then discuss their 4 cases. The first, a man of fifty years, admitted to the hospital for an injury was thought at first to have vagabond's disease because of the dark brown color of the skin. The liver and spleen were not palpable. Glycosuria was present. Autopsy confirmed clinical diagnosis of hemochromatosis. The second was that of a male, aged forty-nine years, in whom symptoms for six months were those of diabetes and during the last two months associated with progressive enlargement of the abdomen. The liver was markedly enlarged. The face was of a dusky hue. The clinical diagnosis was diabetes and carcinoma of the liver. Necropsy revealed the primary malignancy of the liver with hemochromatosis of almost all of the internal organs. The third patient, a male aged fifty-six years, very stupid, was admitted because of pain in the knees. His skin presented a dusky brown color. Abdomen normal, liver and spleen were palpable. A very obstinate nosebleed lasting twenty-four hours occurred. The skin pigmentation increased while under observation. No glycosuria was found. A clinical diagnosis of Addison's disease was made. Necropsy

[1] Archives of Internal Medicine, 1921, **27**, 406.

revealed the hemochromatosis. The fourth patient, a male aged fifty-six years, complained of weakness of the legs and pain in the back. The skin was icteric, the face cyanotic, the legs edematous. The heart examination revealed mitral insufficiency with decompensation. Ascites present. No glycosuria. Clinical diagnosis—none. Necropsy revealed the hemochromatosis.

Acidosis. Each year witnesses an advance in our knowledge of this subject. We are learning that the acid-base equilibrium of the body is remarkably constant; that a low alkali reserve is by no means always an indication of acidosis; that acidosis is not necessarily an indication for the administration of alkalies, etc. The reaction of the blood, the hydrogen-ion concentration, the pH. is dependent on the ratio of alkali to carbonic acid. The reduction in the alkali may be brought about by two opposite processes: Increased production of acids in which alkali therapy is of value (the acidotic process): excessive elimination of CO_2, in which alkali is withdrawn from the blood to the tissues in order to maintain the carbonic acid to alkali ratio (acapnial process). This latter condition is in reality a condition of alkalosis with low blood alkali in which the administration of sodium bicarbonate is dangerous. In this group Henderson and his co-workers maintain that the inhalation of CO_2 properly diluted with air causes a withdrawal of the alkali from the tissues into the blood. Henderson and Haggard[1] believe the acapnial process explains the low blood alkali following anesthesia and surgical operations, and inhalations of CO_2 and not alkali administration are indicated. In keeping with the acapnial conception of anesthesia acidosis is the experience of Healy,[2] who reports serious and even fatal effects of sodium bicarbonate administration after operations. Carbon monoxide asphyxia, according to Henderson and Haggard[3] induces a lowering of the blood alkali by the acapnial, not the acidotic process. The anoxemia induces excessive breathing, and CO_2 is blown off; the decrease in the blood alkali is an attempt at compensation.

In the treatment of carbon monoxide poisoning, Haggard and Henderson[4] point out that in many cases the time when greatest injury is wrought to the nerve centers by the lack of oxygen, is the period of subnormal breathing after removal from the gas-contained atmosphere. When 8 to 10 per cent CO_2 is added to the oxygen inhalations, the breathing in experimental animals is quickly restored to normal, or more than the normal amount. Haggard and Henderson say that with the aid of this full ventilation of the lungs, the mass action of oxygen in the alveoli quickly displaces carbon monoxide from the blood. Certain other changes also occur in the blood, dependent on the restoration of its carbon dioxide and the recall of alkali from the tissues. Thus, in ten or fifteen minutes the subjects (dogs) are on their feet, virtually restored. In this treatment, Henderson and Haggard believe that they have the long sought for ideal therapy for carbon

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[1] Journal of the American Medical Association, 1920, **74,** 783.
[2] American Journal of Obstetrics and Gynecology, 1921, **2,** 164.
[3] Journal of Biological Chemistry, 1921, **47,** 421.
[4] Journal of the American Medical Association, 1921, **77,** 1065.

monoxide poisoning which will be effective if the exposure to carbon monoxide has not been long enough to permanently damage the body cells as a result of the anoxemia.

Reimann and Reimann[1] and Reimann and Sauter[2] studied the blood bicarbonate following the administration of sodium bicarbonate. When sodium bicarbonate is given by mouth in normal individuals the highest point in the blood bicarbonate occurs in approximately from one and a half to two hours. The comparison of results obtained was surprisingly close to those estimated in advance by the Palmer-Van Slyke formula. In a series of 25 patients with various diseases, the values obtained compared to the calculated values, show a deviation greater than the normal. Although the number of cases studied by Reimann, and his co-workers, are so few as to preclude conclusions, further investigation is suggested. Following the intravenous injection in animals of a 4 per cent sodium bicarbonate solution, Reimann and Sauter found that there was a parallel increase in the blood and lymph bicarbonate and that the bicarbonate left the blood for the lymph at a remarkably rapid rate.

The alkali reserve of the blood plasma during protein shock was studied by Eggstein,[3] who found a relationship between the decrease in the reserve and the lowered blood pressure incident to the shock. The administration of sodium bicarbonate before the injection of the protein retards the fall of the blood alkali to a critical point. Sodium bicarbonate given during the protein shock relieves distressing symptoms. Eggstein states that acute anaphylactic shock in dogs is associated with immediate and progressive acidosis. When the carbon dioxide capacity of the plasma falls below 25 per cent, the animal usually dies. If the animal survives, acidosis is quickly relieved. The administration of sodium bicarbonate before the anaphylactic shock has a beneficial effect, although it will not always prevent death, even though the alkali reserve is restored to normal.

In acidosis there occurs a reduction in the carbon dioxide capacity of the blood plasma. Peters and Barr[4] studied the CO_2 absorption curve of the blood in 7 patients with cardiac decompensation and dyspnea and in 6 patients with severe anemia. Among the cardiac patients, 3 were found with low curves. In the patients with anemia, the curve had a flatter slope than normal. In 2 of the 3 cardiac cases, the curves returned to the normal level when compensation was re-established. In the cardiac cases the reduction of the alkali reserve indicated by these low absorption curves was not reflected in the plasma. The carbon dioxide capacity of the venus plasma is determined by the carbon dioxide tension existing in the body, rather than the combining capacity of the blood. In 4 cases the carbon dioxide tension of the arterial and venus blood was determined with the finding of a definite retension with a lowering of the hydrogen-ion concentration in 2 cases.

[1] Journal of Biological Chemistry, 1921, **46**, 493.
[2] Ibid., 1921, **46**, 499.
[3] Journal of Laboratory and Clinical Medicines, 1921, **6**, 481 and 555.
[4] Journal of Biological Chemistry, 1921, **45**, 537 and 571.

In all 4 cases there was a difference between the alveolar and arterial carbon dioxide tension varying from 13 to 19 mm.

Peters and Barr summarized the causes of cardiac dyspnea as follows: The fact that a greater ventilation is necessary to effect the normal carbon dioxide elimination. This is largely brought about by an impairment of the efficiency of the pulmonary mechanism for the exchange of gases between the blood and the outside air. This necessitates the maintenance of a greater difference in carbon dioxide pressure between the blood in the pulmonary circulation and the alveolar air in order to effect the normal carbon dioxide output. To maintain the carbon dioxide tension and the hydrogen-ion concentration at the proper level, the alveolar carbon dioxide tension must be abnormally low. In some cases a diminution of the circulation rate may be an additional factor in the production of a carbon dioxide acidosis. Finally, in a certain proportion of the cases, at least, there is a real reduction of the available alkali of the blood. In at least 2 cases with a reduction of the available alkali of the blood were found indications of a comparative insensibility of the respiratory center to its natural physico-chemical stimulus, the hydrogen-ion concentration of the blood.

As stated above, Peters and Barr also studied the CO_2 absorption curves of blood from 6 patients with severe anemia. These curves were found to have a flatter slope than the curves of normal blood. This is explained in part by the low percentage of hemoglobin, although the flatness of the curves is not exactly proportional to the hemoglobin diminution. The blood of severe anemia has a diminished power of absorbing or dissociating CO_2, with changes of CO_2 tension. Absorption of CO_2 from the tissues, or loss of CO_2 from the lungs, is probably accomplished with difficulty. In all the cases the venous hydrogen-ion concentration was surprisingly constant, while the arterial blood hydrogen-ion concentration was found relatively low in 3 of the cases. In spite of the relatively small difference in CO_2 content between arterial and venous blood, the corresponding difference in the hydrogen-ion concentration was considerable. This is due to the flat absorption curve and the loss of the compensating effect of oxygen unsaturation. In severe anemia, changes in CO_2 tension produce relatively small changes in CO_2 content, and relatively great variations in hydrogen-ion concentration. The fault in the CO_2 carrying power and the greater changes in hydrogen-ion concentration may explain the dyspnea of anemia.

In 1916, Howland and Marriott called attention to the occurrence of *acidosis in infants with severe diarrhea*. The depletion of the alkali reserve is not a cause of the diseased condition, but is caused by the condition producing the diarrhea. The excessive loss of alkali by the bowel causes an upset in the carbonic acid-alkali ratio of the blood, with an increase in the hydrogen-ion concentration; the rapid respiration with blowing off of the carbon dioxide acts as a compensatory measure. Guy[1] calls attention again to this subject. He states that the alkali

reserve can be increased to normal, the hyperpnea controlled and the general toxic symptoms alleviated by the administration of sodium bicarbonate, but that the ultimate outcome is but little influenced by this treatment. Guy believes that there must be some toxic acid produced which continues its pathological activity even when neutralized, and that specific therapy awaits its discovery. There is, of course, the other view mentioned above, which offers to explain the acidosis on the basis of loss of alkali by diarrhea.

The *nature of acidosis in nephritis* is discussed by Mason.[1] The acidosis in nephritis is distinctly a "retention" acidosis, as distinguished from the acidosis (or more properly termed ketosis) found in diabetes, starvation, and vomiting of pregnancy. In nephritis, there is frequently marked dyspnea due to inability on the part of the body to maintain the normal ratio, with the result that the blood contains more ionized hydrogen than normally. Treatment of acid retention in nephritis depends upon a passive restoration of the bicarbonate reserve by means of the administration of sodium bicarbonate by mouth, rectum, or other channels, combined with the usual means of reëstablishing kidney function. In most cases it is not difficult to raise the carbon dioxide capacity of the blood to a normal level, but it is more difficult to stimulate the kidneys to eliminate the acid phosphates. The alkali therapy should be properly controlled, as it is not without danger generally, and especially when there is impaired kidney elimination. There is danger of alkalosis associated with symptoms of tetany.

The *nomenclature* of the whole subject of acidosis presses for revision, according to Evans,[2] who discusses our modern conception of the reaction of the blood and the mechanism of its regulation. Naunyn introduced the term acidosis for the formation in metabolism of large amounts of non-oxidizable organic acids. As Poulton[3] points out, oxybutyric acid forms the most notable example; and the excessive production of lactic acid in diseases of the liver is one of several other examples. In the use of the word there was no suggestion that oxybutric acid necessarily acted by making the blood acid; in fact, controversy raged for many years as to whether coma was produced in this way, or whether the acids were poisonous in themselves. It is fairly certain now that the latter is the correct alternative, aceto-acetic acid being the poisonous substance. After Naunyn, Barcroft was among the first to use the term acidosis to mean an increase in the acid relative to the basic radicals in the blood. He drew a distinction between the hydrogen-ion concentration and alkali reserve of the blood. Van Slyke and Cullen, in 1917, introduced the phrase, "diminished alkaline reserve." Evans[4] points out that a little reflection on the mode of regulation of the reaction of the blood suffices to reveal a difficulty which is becoming daily more apparent: Lowered bicarbonate content of the plasma by itself, or lowered alveolar carbon dioxide by itself, gives no information at all regarding the reaction of the blood; yet

[1] Canadian Medical Association Journal, 1921, **2,** 424.
[2] Lancet, 1921, **201,** 867.
[3] British Medical Journal, 1921, **1,** 508.   [4] Ibid.

these are often accepted as evidence for the existence of a state called "acidosis." Nor does the plea that the term "acidosis" is justified in these cases on the ground that there is evidence that fixed acids have been formed and that these have neutralized part of the bicarbonate, carry any weight, because an increased excretion of alkali by the kidneys would also lead to a reduction in the plasma bicarbonate. A more acid state of the blood can only be inferred from such observations when we know both the carbon dioxide pressure and the bicarbonate content of the arterial blood, and the former can only be obtained from alveolar air analyses when it is certain that there is complete equilibrium between the alveolar air and the arterial blood; this certainty is lacking in many pathological conditions.

Haldane[1] also points out that confusion will result if acidosis is considered as synonymous with diminished "alkaline reserve." It is now clearly established that the "alkaline reserve" may be, and often is, diminished in cases in which the blood is abnormally alkaline; and, conversely, that the "alkaline reserve" may be increased where the blood is deficient in alkalinity. The expression "alkaline reserve" is an unfortunate one, insofar as it suggests the existence of a reserve of alkali beyond what is required to maintain a normal reaction. In actual fact the whole of the normal "alkaline reserve" of the blood is required to balance the carbonic acid normally present. When less or more carbonic acid than usual is present, the "alkaline reserve" is gradually diminished or increased to such an extent as nearly to restore, if possible, the normal reaction. Conversely, if the "alkaline reserve" is increased or diminished, the carbonic acid in the blood is, by diminution or increase of the breathing, so increased or diminished as, if possible, nearly to restore the reaction. Haldane suggests that for "alkaline reserve" one might substitute some such expression as CO_2 combining capacity. The former will probably survive, as it is now so extensively used. To define acidosis, or alkalosis, as diminution or increase in "alkaline reserve," is, however, so definitely misleading that Haldane believes such a definition should be avoided. Acidosis and alkalosis are extremely small, but also extremely important, deviations from normal in the hydrogen-ion concentration within the body. The available direct physical and chemical methods are still too rough to enable us to follow these deviations closely, but we can do so by the far more delicate method of observing the accompanying changes in breathing and in the excretion of acid or alkali and ammonia by the kidneys.

THE DUCTLESS GLANDS.

Endocrinology. Hoskins[2] makes a very timely plea for conservatism in this most difficult field; a conservatism which will prevent our being carried away by fantastic theories and yet allow of the proper estimate of well-worked-out experimental and clinical studies. Some of the current trends in endocrinology reveal, according to Hoskins, two

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[1] British Medical Journal, 1921, **1**, 542.
[2] Journal of the American Medical Association, 1921, **77**, 1459.

groups of practitioners: One in which endocrinology betokens a mass of extravagant absurdities on a par with phrenology or mesmerism, to the other it betokens a new gospel, the light of which is destined to guide medicine to glorious heights. The first class dismisses with a shrug the work of such men as Kocher, Minkowski, Biedl, Hammar, Schafer—to mention only a few of those to whom endocrinology is most indebted. The second class betrays a remarkable obliviousness to the history of fashions in medicine. Both classes, the ultraconservative and the ultrasanguine, are exerting an influence detrimental to further progress.

An editorial[1] comment points out the need of conservatism in the use of the endocrines in therapy. There is a real danger in the indiscriminate acceptance of data supplied by various commercial houses. The exploitation of ductless gland therapy is often associated with unwarranted claims of brilliant therapeutic results. In a general way, it is well to remember that the relation of endocrinology to sound therapeutics is still largely undetermined, and, until more information is obtainable from reliable sources, honesty as well as prudence demands caution and circumspect discrimination.

From the point of view of endocrine diagnosis, a word of caution would seem timely. Some enthusiasts are prone to formulate a fabric of endocrine syndromes based on specious reasoning. One is reminded in reading over the current literature of the endocrines of some of "the facts and fancies regarding uric acid" through which medicine emerged in the past. Many of these syndromes are arm-chair deductions based on our incomplete knowledge of endocrine physiology. The complexity of many of these syndromes is, in itself, evidence of their uncertainty. The reviewer does not wish to convey the impression that he is an obstructionist to medical progress, but rather wishes to discourage the "shallow theorizing on the part of those dabbling in the problems." To quote Hoskins again, there is no easy road in endocrinology, either to discovery or to knowledge already gleaned. On the other hand, it would be unfortunate to assume that none but supermen can hope to bring forth significant results. There are many problems demanding solution, which require, not genius, but merely accuracy and patience, together with recognition of the ordinary criteria of evidence in any field.

THE THYMUS

Status Thymico-lymphaticus. The necropsy experience among soldiers has shown, according to Sternberg,[2] that our views concerning status lymphaticus, lymphatism, etc., require revision. According to Borst and Grace, whose observations were based on necropsies on over 2000 men who had been killed in action, lymphatic hyperplasia was found in 56 per cent of all soldiers and in 86 per cent of those aged nineteen to twenty. These striking findings, according to Sternberg, reveal that we have not in the past realized the normal state of the lymphatic

[1] Journal of the American Medical Association, 1921, **77**, 1499.
[2] Wien. klin. Wchnschr., 1921, **34**, 291.

tissues. In young persons the lymph nodes are, normally, extremely well developed, and hitherto a lymphatic state was assumed simply because the normal condition was not understood. The lymphatic tissue disappears with increasing age and as the result of various diseases and nutritional disorders. In necropsies on persons who die in hospitals, the lymph glands are generally small and so give a false idea as to the normal condition. On the other hand, in young persons who die a violent death a well-developed lymphatic tissue represents a normal condition. Sternberg does not deny that in some persons, even in advanced life, there may be an unusual development of the lymphatic tissue accompanied by other anomalies, especially vascular hypoplasia. Such cases, however, to which the term "status lymphaticus" is really applicable are rare and have nothing to do with the condition which is commonly called lymphatism.

Yamanoi[1] investigated the condition of the 303 patients over twenty-five years of age, dying of influenza. In 26 plus per cent of 187 men and in 20 plus per cent of 116 women, there was evidence of persisting thymus. It is evident that we must cease regarding macroscopic thymus tissue as an evidence of abnormality.

The enlargement of the thymus seen in infancy has of course been regarded as normal. Blackfan and Little[2] state that a thymus large enough to demonstrate by percussion and to show in the roentgen-ray plate, does not necessarily give rise to symptoms. That enlarged thymus may produce symptoms *per se* is evidenced by the relief afforded by direct roentgenization of the gland. On the other hand, as pointed out by Ladd,[3] one must keep in mind that the symptoms may be due to an internal secretory defect, rather than to pressure.

Timme, in an address before the Philadelphia Nuerological Society, called attention to the clinical manifestations and frequency of status thymicus and stated that but few of the patients die the sudden death which we are prone to consider as the important manifestation. Many show pituitary, thyroid, adrenal and other disturbances brought about by the effort on the part of these endocrine glands to compensate for the hypoplasia, local and general, which is part of status thymico-lymphaticus. The thymico-lymphatic state is one of widely differing manifestations. Timme[4] states that the pituitary gland is usually small and encased in a sella turcica which is likewise small and enclosed by the clinoid processes. The symptoms are fatigue, dyspnea on exertion, fainting attacks and collapse in critical situations, syncope and death in narcosis, fright and exhaustion. Death is due to adrenal exhaustion. Urticaria, asthma, acidosis, hay fever, enuresis, circumscribed edema and arthritides are concomitants. The blood pressure is low, the pulse pressure frequently being down to 10 or 15 mm. Throbbing periodical headaches following fatigue occur as a result of pituitary disturbance. In tracing the evolution from status thymico-lymphaticus, Timme states that in a given case one to three years

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[1] Schweizerische medizinische Wochenschrift, 1921, **51**, 557.
[2] Journal of the American Medical Association, 1921, **77**, 312.   [3] Ibid., 312.
[4] New York Medical Journal, 1921, **114**, 12.

following the period of constantly recurring headaches, the blood pressure, pulse pressure and blood sugar are higher, the skeletal growth has increased and the sella turcica has enlarged. Pituitary hyperactivity has occurred and as this compensatory process proceeds, the headaches grow less intense and symptoms of hyperpituitarism develop. If a small sella resists enlargement, pituitary treatment will probably be needed throughout life. If the pituitary fails to compensate, there is a frequent association of mental disturbances of the types producing liars, kleptomaniacs, moral inferiors and drug habitues.

Timme states further that, in the treatment of these patients, thyroid with iodine is indicated. If the thymus remains large, the roentgen ray should be used. Suprarenal gland sometimes helps, but adrenalin does not. A well-ordered life, with the avoidance of physical and mental strain, is essential in the care of these patients.

Epitheliomas of the Thymus. It is possible, according to Symmers and Vance,[1] to divide the tumors of the thymic parenchyma into two groups—the members of one group springing from the preponderating cell of the adult thymus, namely, the lymphocyte; the members of the other group arising from that cell which originally dominated the thymus, but which, as development proceeds, is projected into the background, that is to say, the epithelial cell. Only three examples of primary thymic epithelioma are to be found in the literature. A fourth is recorded in this paper. The patient was a man, aged fifty-eight years, a painter by occupation, who was admitted to the hospital June 26, and died four months later. At the time of admission, the patient complained of severe burning pains in the back that had been present for three weeks. Three days before admission these pains became so excruciating that he was unable to stand and had to give up work and take to his bed. In addition, he complained of pain in the upper sternal region on swallowing. The entire dorsal spine was rigid and this rigidity was increased by movements of the trunk. Two weeks later the patient could not move the body below the waist. The superficial reflexes were abolished, while the knee-jerks were preserved, and he was sensible to pain up to a girdle point about 5 cm. above the lower border of the ribs. On the following day there were complete paralysis and anesthesia of the entire body below the level corresponding to the fifth dorsal segment. The patient now complained of no pain except when the head was moved, at which time pain was severe and was referred to the region between the fourth and sixth dorsal vertebræ, where there was also tenderness on pressure. The knee-jerks had disappeared and there was a bilateral Babinski. The patient suffered from retention of urine and incontinence of feces. The spinal fluid was yellowish in color and contained 30 cells to the cubic millimeter. Examination of the urine revealed nothing of note. The Wassermann reaction was negative.

About three weeks after admission the spinal column was opened from the fourth cervical to the second dorsal vertebra, and a tumor

[1] Archives of Internal Medicine, 1921, **28**, 239.

was removed from the dura mater corresponding to the region between the sixth cervical and the second dorsal vertebra. The growth measured 6 x 2½ cm. and pressed on the dorsal cord. In the succeeding three months the patient gradually failed, bedsores developed, and death occurred October 25. Except for pain on swallowing, the patient at no time during his stay in the hospital exhibited signs or symptoms referable to pressure in the anterior mediastinum. At necropsy, on opening the thorax, a mass came into view corresponding to the position of the thymus. The mass measured 10 x 8 x 3 cm., and was roughly triangular in outline, with the base upward. The growth was milk-white in color and of cartilaginoid consistence, and was attached to the border of the left lung for a distance of about 6 cm. Scattered through the left pleura were a few firm nodules, varying in size from ½ to 1 cm. The tissue composing these nodules was quite similar to that of the mass in the thymic region. On section, both lungs were studded with nodules of similar description. The heart was not displaced. The transverse portion of the arch of the aorta passed immediately behind and was partially included in the tumor lying in the thymic region. The aorta itself, however, was not infiltrated.

Symmers and Vance state that, from the clinical standpoint, tumors of the thymic parenchyma, both epithelial and lymphocytic, present certain features of practical interest. First, the lymphocytic tumors outnumber the epithelial by a considerable margin. Moreover, the lymphocytic tumors in the majority of cases occur in individuals under thirty-five years of age, many of them in children, while all of the few epithelial tumors that have been recorded occurred in persons over fifty years of age. Second, there are considerable variations in the matter of physical signs. For example, (a) certain tumors of the thymic parenchyma grow expansively in the upper thorax for long periods of time without giving rise to noteworthy signs of pressure. These growths represent a minority, it is true, but that they exist is shown by the presence of a comparatively trivial complaint in the case recorded, namely, pain on swallowing. (b) Others grow expansively in the upper thorax and are attended by marked signs of pressure, such as cough, expectoration, dyspnea, cyanosis and edema, particularly of the right side of the chest anteriorly and of the corresponding arm, due to interference with the circulation in the innominate and subclavian veins; hydrothorax, ascites, and the like. A subdivision of this group is represented by those thymic lymphosarcomas which grow expansively for a period of months or years, and suddenly terminate life with the picture of acute leukemia, the tumor pouring lymphocytes into the circulation abruptly and in large numbers—the so-called leukosarcoma of Sternberg.

As Symmers concludes, the growing attention to thymic tumors makes it not impossible that with an early diagnosis some of these growths may be discovered before neighboring tissues have been irreparably damaged. The preponderance of lymphoid growths of the thymus and the known effects of radiation on lymphocytic tissues suggest that the use of the roentgen ray might be beneficial in the

treatment of tumors of this type. Also, it is conceivable that greater attention to the interpretation of symptoms of pressure in the anterior mediastinum, coupled with such diagnostic aids as the roentgen ray, might sometimes lead to detection of thymic tumors sufficiently early to permit of their enucleation before they have progressed too far.

THE THYROID GLAND.

The Thyroid. Function. Goiter. In discussing the interrelationship of the function of the thyroid gland and the tissures of the body. Plummer[1] calls attention to the only known specific function of the gland, namely, the production and storage of thyroxin. This substance is active directly or indirectly in the cells in the tissues throughout the body. The thyroid gland is a potent factor in maintaining the normal basal metabolism at a given rate. Plummer states that we may assume without knowing the exact mechanism of the normal thyroid stimulation that it is brought into play by a drop in the amount of thyroxin in the tissues of the body. This being true, the daily administration of 1 mg. or more of thyroxin should place the thyroid at partial or complete rest, at least so far as the production of this agent is concerned. Following this hypothesis, the daily administration of from 0.5 to 1 mg. of thyroxin to a normal person might not be attended by any general physiologic reaction. A daily oral dose of 1.6 mg. of thyroxin will hold the basal metabolism of most thyroidless individuals within the normal limits. In most instances the dose established two or three years ago has not had to be changed, the basal metabolism estimates being within 5 per cent of the average normal each time the patient has returned for observation. A daily dose of from 2 to 3 mg. of thyroxin or 20 gms. of desiccated thyroid given by mouth will not fluctuate the basal metabolism or cause any physiologic reaction in many patients in whom this dose given intravenously causes the quantitative reaction almost standard for myxedematous patients. In isolated cases, 250 gms. of desiccated thyroid has not caused any reaction. This failure of absorption or destruction of thyroxin before reaching the general circulation is characteristic of a considerable percentage of patients who have diffuse colloid goiter and of patients in the various groups having low basal metabolism readings not attributable to a primary hypothyroidism. This failure of absorption, the difficulty of carrying out daily intravenous administration over a long period, the probability that the thyroid is placed at partial or complete rest, and evidence that under certain conditions the thyroid picks up and stores part of the thyroxin, have been most baffling in the attempt to study quantitatively the reactions of persons having functioning thyroids.

The relation of edema to hypothyroidism and other states causing a lowered basal metabolism is discussed by Plummer. He states that the edema of myxedema develops, or at least becomes recognizable, when the basal metabolism drops from 15 to 17 per cent below the average

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[1] Journal of the American Medical Association, 1921, **77**, 243.

normal. In a myxedematous person having a basal metabolism ranging near this point, the edema may appear after stress, and disappear after rest. Sustained stress exhausts the thyroxin more rapidly than it can be produced by the thyroid and the basal metabolism drops a few points. A recognizable edema may disappear and reappear with a shift of 1 mg. or less of thyroxin in the tissues of the body. A drop in the basal metabolism to 40 per cent below normal does not cause edema in the classifiable and unclassifiable conditions not due primarily to hypothyroidism. This relation of edema to the basal metabolism is of the highest significance in the differential diagnosis of primary hypothyroidism and of the other conditions with which a low metabolism is associated.

In another interesting paragraph, Plummer points out how easily it is to confuse the phenomena attending an elevation of the metabolism and an increased rate of exhaustion of thyroxin in the tissues from stimulation originating in the central nervous system and the resulting evidence of stress on the thyroid with the phenomena of hyperthyroidism. It is apparent when we recognize that but for the transformation of part of the energy to motion, the phenomena of physical exertion and the resulting fatigue can be distinguished only with difficulty from those of pure hyperthyroidism. The phenomena of mild exophthalmic goiter are so much like the psychoneurotic manifestations due to lack of assurance that the thyroid is frequently resected for the latter condition.

Plummer's paper is full of interesting comments. He states that goiters usually classified under the terms "simple," "endemic," "adolescent," and so forth, are diffuse colloid, adenomatous, or a combination, particularly at their inception, of the two types. The majority of such goiters are first noticed during the latter half of the second decade. The colloid goiter usually disappears before the twenty-fifth year; however, there is a tendency for a thyroid once overloaded with colloid, irrespective of its functional activity, to retain more than the normal amount, that is, sufficient to make the gland easily palpable throughout life. The adenomatous nodules often during the early part of their history, in colloid goiter, never disappear, although they fluctuate much in size with their colloid content, vascularity, and degenerative changes.

The administration of iodine may prevent the formation of colloid goiter. That it may also be almost equally efficacious in the prevention of adenomatous goiter in adolescence seems probable. Two theories have prevailed with regard to hyperfunctioning adenomatous goiter: First, that the adenomatous tissue elaborates and delivers an excess of thyroxin, and second, that the adenoma in some way stimulates the surrounding thyroid tissue to hyperfunction. Though the question must still be considered open, the evidence correlates best with the theory that the adenomatous tissue hyperfunctions. Plummer states that the development of diffuse colloid goiter in man, other factors remaining constant, is determined by an equation taking into consideration the iodine available to the thyroid and the rate of exhaustion of thyroxin in the tissues. Infection of the organism, at least when

attended with fever, probably increases the rate of exhaustion of thyroxin in the tissues. That infection of the thyroid can stimulate the gland to hyperfunction is indicated by a moderate degree of hyperthyroidism early in the history of patients having diffuse thyroiditis ultimately resulting in myxedema. That introduction of bacteria into the digestive tract is an important factor, if not the primary cause of endemic goiter, is fairly well established. As to how the organisms act in the host, there is no definite evidence. That the bacterial flora of the digestive tract may sufficiently interfere with the absorption of the small amount of iodine in the available diet is a possibility, particularly in areas in which this element is relatively small. The relation of the bacterial flora to the available iodine would well explain the geographic distribution of endemic goiter.

The prevention of simple or endemic goiter in man may be achieved by the administration of 3 to 5 mg. of iodine twice weekly over a period of a month, and repeated twice yearly. Marine and Kimball[1] again call attention to their observations in Akron, Ohio. These observers believe that the ultimate cause of simple goiter is totally unknown, notwithstanding a relatively large amount of study. The immediate cause is a lack of iodine. The enlargement, therefore, is a symptom and may result from any factor which increases the iodine needs of the organism, as in certain types of infection, or which interferes with the normal utilization of iodine. In other words, thyroid hyperplasia (goiter) is a compensatory reaction arising in the course of a metabolic disturbance and immediately depending on a relative or an absolute deficiency of iodine.

Proceeding from carefully-controlled animal experimentation to human studies, Marine and his co-workers attempted "goiter prevention" among school children of Akron. They gave 2 gm. of sodium iodide in 0.2 gm. doses, distributed over a period of two weeks each, spring and autumn, *i. e.*, twice yearly. The results of two and one-half years' observation on school girls are as follows: Of 2190 pupils taking 2 gm. of sodium iodide twice yearly, only 5 have developed enlargement of the thyroid; while of 2305 pupils not taking the prophylactic, 495 have developed thyroid enlargement. Of 1182 pupils with thyroid enlargement at the first examination who took the prophylactic, 773 thyroids have decreased in size; while of 1048 pupils with thyroid enlargement at the first examination who did not take the prophylactic, 145 thyroids have decreased in size. These figures demonstrate in a striking manner both the preventive and the curative effects.

Klinger[2] has recently reported even more striking curative results in the school children of the Zurich district. He worked with school populations in which the incidence of goiter varied from 82 to 95 per cent, while the maximum incidence in Akron was 56 per cent. With such a high natural incidence of goiter, his observations necessarily deal more with the curative effects. Thus of 760 children, 90 per cent were goitrous at the first examination. After fifteen months' treat-

[1] Journal of the American Medical Association, 1921, **77**, 1068.
[2] Schweizerische medizinische Wochenschrift, 1921, **51**, 12.

ment with from 10 to 15 mg. of iodine weekly, only 28.3 per cent were goitrous, of a total of 643 children reëxamined. While the thyroid enlargements developing around the age of puberty are more common, they are not more important than those developing during pregnancy and fetal life. The thyroid enlargement of both mother and fetus may be prevented by giving 2 gm. of sodium iodide, or its equivalent in iodine in any other form, during the first half of pregnancy. The dangers of giving iodine, in the amounts indicated, to children and adolescents are negligible. No case of exophthalmic goiter developed in the series reported by Klinger or by Marine and Kimball, although in both instances such cases were carefully looked for. Marine and Kimball conclude that if the prevention of goiter is good preventive medicine, it is better preventive surgery. With so simple, so rational, and so cheap a means of prevention at our command, this human scourge, which has taken its toll in misery, suffering and death throughout all ages, can and should be controlled, if not eliminated.

Centers of endemic goiter are numerous throughout the world and in such centers the application of the knowledge gained from the observations of Marine and Kimball ought to be of the greatest good. For example, a reference in the past year was made to the frequency of endemic goiter in certain parts of Mexico. Nájera[1] found 20 to 25 per cent of the population so affected in parts of the state of Guerrero.

Levin,[2] working in a goiter zone, examined 1783 persons ranging in age from newborn to sixty-one years of age for enlarged thyroids. He found 1146 enlarged thyroids, of which 682 were simple goiters, 420 adenomas and cystomas and 44 colloid goiters. The incidence curve shows that goiters increase in both sexes during puberty, dropping to a small degree after the growth of the individual is attained. The curve remains in the female for the child-bearing period, going down at about thirty-eight or forty years, when it rises again for the menopause. In the male the curve gradually drops until thirty-five or forty years, when there is a small rise due to the growths in the glands asserting themselves, the male having no special metabolic change to influence the enlargement. The simple goiters maintain the high percentage until thirty-five years is attained and the adenoma and cystoma sustain the height of the incidence curve after that age. Levin directs attention to the fact that in a zone in which thyroid enlargements occur, there is a normal physiologic hypertrophy, and this should not be called goiter.

Acute Thyroiditis. Four cases of suppurative thyroiditis requiring incision are reported by Edwards.[3] All of the patients recovered and have remained entirely well and without evidence of hyper- or hyposecretory activity of the gland. In 3 of the 4 cases, the infection followed a respiratory inflammation; and in the fourth case, while the thyroid complication was coincident with an abdominal inflammation, there was also a very transient and mild inflammation of the pharynx. The

[1] Revista Méxicana de Biologia, 1920, **1**, 47.
[2] Archives of Internal Medicine, 1921, **27**, 422.
[3] Journal of the American Medical Association, 1921, **76**, 637.

onset of the symptoms is usually sudden. There is pain in the neck, frequently referred to the ear, teeth, shoulder, arm or chest, depending on the amount of pressure produced by the inflammation and, furthermore, on the toxic effect of the microörganism. This is associated with an elevation of temperature and a rapid pulse, a persistent cough with pronounced changes in the voice, dyspnea, which at times may be so severe as to require tracheotomy, painful swallowing and extreme restlessness. The leukocyte count is usually increased. The physical examination reveals exquisite tenderness over the anterior portion of the neck below the larynx. There is usually swelling, which may be localized or diffuse; redness and a marked induration, which sometimes makes it difficult to differentiate from woody phlegmon. There is usually rigidity of the muscles of the side affected, so that if only one lobe is inflamed, the head will be turned toward that side. Palpation of the gland is usually unsatisfactory because of the pronounced tenderness.

Gilman[1] reports a case of acute suppurative thyroiditis in a laborer of thirty-nine years of age, who complained of swelling, stiffness and pain in the neck of five days' duration. He had had influenza a short time previously. His temperature was 101° F., his pulse 120; he had a severe headache, hoarseness and cough. Under a general anesthetic and incision, 1 to 2 ounces of creamy pus were evacuated. Cultures of the pus revealed a Type I pneumococcus. The patient made an uninterrupted recovery.

Hyperthyroidism and Hypothyroidism. Functional Tests. During the past few years considerable interest has centered around the use of various functional tests as aids in the diagnosis and treatment of thyroid disorders. The three most important of these tests are: (1) the basal metabolism, (2) the glucose tolerance, and (3) the epinephrin hypersensitivity test. With regard to the first, the basal metabolism, we will deal later. With regard to the *glucose tolerance* or *alimentary hyperglycemia* test, Morris[2] found it of distinct value in the diagnosis of mild hyperthyroidism, although not pathognomonic. Morris's conclusions confirm the work of Denis, Aub and Minot and others previously reported. Morris studied the test in a group of patients of the so-called borderline type. In these patients, whose symptoms and physical findings are suggestive but insufficient to warrant the making of a positive diagnosis of hyperthyroidism, the obtaining of results similar to those recorded in the ten cases reported may be considered as valuable corroborative evidence of the presence of thyrotoxicosis.

Adrenalin hypersensitiveness and its relation to hyperthyroidism was studied by Peabody, Sturgis, Tompkins and Wearn.[3] This test, it will be recalled, consists of the injection of 0.5 cc of a 1 to 1000 solution of adrenalin, which in the presence of hyperthyroidism is supposed to give such positive signs as a rise of systolic blood pressure

[1] California State Medical Journal, 1921, **19**, 294.
[2] Journal of the American Medical Association, 1921, **76**, 1566.
[3] American Journal of the Medical Sciences, 1921, **161**, 508.

of at least 10 mm. of mercury or a rise in pulse-rate of at least 10 beats per minute, together with an increase of such signs and symptoms as tremor, sweating, vascular pulsation, nervousness and palpitation. The test is so easy to apply and apparently so simple to interpret that it has been widely adopted as a diagnostic measure, and the "positive" reaction is frequently considered as an indication even for surgical interference.

After a very careful study of the test, Peabody, and his co-workers, state that hypersensitiveness to adrenalin is found in many patients with the clinical picture of hyperthyroidism and with an increased basal metabolism, but it is not constant under these conditions. Hypersensitiveness to adrenalin is also found in persons who have no indications of hyperthyroidism. Thus it was present in many psychoneurotics, in about 50 per cent of patients convalescent from acute infections, in nearly the same proportions of soldiers with "effort syndrome," in 14 per cent of apparently normal young men and in patients with various unrelated diseases. The "positive" reaction to adrenalin appears to occur most often in highly nervous individuals, but it is not constant in such persons. The clinical significance of the reaction is not clear, but at present it should certainly not be regarded as having any specific significance in the diagnosis of hyperthyroidism.

Russell, Millet and Bowen[1] made a study of the thyroid function tests, *i. e.*, the adrenalin sensibility, glucose tolerance and basal metabolism in a group of 85 cases showing symptoms either definitely attributable to disturbance of the endocrine glands, particularly the thyroid, or not readily explainable on any other basis. The cases studied were divided into four groups: Hyperthyroid, hypothyroid, fatigue and a large miscellaneous group. Clinical methods were found satisfactory in the diagnosis of frank hyperthyroidism, myxedema and to a lesser extent in the third and fourth groups. In apparent hypothyroidism—not myxedematous in type, however—the ordinary clinical methods usually failed to suggest the probable diagnosis. In such cases the diagnosis was made entirely on the basis of a decreased basal metabolic rate, together with definite improvement after the administration of thyroid extract. Of the functional tests used, the basal metabolism was the only one to yield uniform results, which could be reasonably interpreted in association with the clinical findings and subsequent progress of the cases studied. An apparatus for the determination of the basal metabolic rate is indispensable in a diagnostic clinic. This test affords the best index of the degree of thyroid activity. Both of the other tests yielded positive results in almost all cases of hyperthyroidism, but the frequency of similar responses in a variety of other conditions, in some of which the diagnosis of hyperthyroidism was not even a remote possibility, necessarily detracts from their value as specific tests of thyroid function.

Special emphasis is laid on three points brought out by the data presented. These are: (1) That there are some cases showing definite

hypersensitiveness to adrenalin and intolerance to glucose which tolerate thyroid extract well and improve under its administration; (2) that it is dangerous to attribute much importance to a positive adrenalin response in the diagnosis of suspected hyperthyroidism; and (3), a corollary of the point just mentioned, that an occasional case of classical exophthalmic goiter showing marked increase of the basal metabolic rate may exhibit no hypersensitiveness to adrenalin.

BASAL METABOLISM. The simplification of the apparatus for determining the basal metabolism has made it possible for many to make observations in this field. Benedict[1] cautions in a timely way against hasty conclusions in the interpretation of basal metabolism estimations by new workers in the field. He states that it is possible for a tyro to secure measurements which frequently neither he nor his associates are in a position to interpret intelligently, and from which it is possible for him to draw deductions that are not only erroneous but, since they not infrequently may influence for or against operative procedure, may actually be of serious harm. The importance of basal metabolism studies in the handling of thyroid cases is generally recognized. As Rowe[2] states, these determinations aid us greatly in the diagnosis of early and obscure cases of hyperthyroidism. It enables us to determine not only the degree of thyrotoxicosis, but is a valuable guide in treatment of hypothyroid states. In the diagnosis of hyperthyroidism and in directing and gauging thyroid administration the metabolic rate determinations are of the greatest importance.

Monthly fluctuations in the metabolic rates of women occur about the menstrual time. Rowe and Eakin[3] confirm the results obtained by previous investigators that "a rather constant rise during menstruation occurs, or in the premenstrual period, the rise being followed by a postmenstrual fall." Wiltshire[4] studied 5 subjects during the menstrual period, as well as during the intermenstrual period. The results he obtained showed that the basal metabolism was not appreciably affected by menstruation. Blunt and Dye[5] made 216 observations on the basal metabolism of 17 women. They conclude that there is no definite change in the basal metabolism during menstruation.

The metabolism of man in the tropics is discussed by Eijkman[6] who states that the inhabitants of hot climates have a basal metabolism not perceptibly lower than the inhabitants of temperate climates. One subject in particular had a basal metabolism which was identical during a stay in Batavia and after ten months when he had returned to Holland.

Basal metabolism estimations furnish the best measure for gauging the effect, according to Mosenthal,[7] of roentgen ray, medication, or

[1] Journal of the American Medical Association, 1921, **77**, 247.
[2] American Journal of the Medical Sciences, 1921, **162**, 187.
[3] California State Medical Journal, 1921, **19**, 320.
[4] Lancet, 1921, **201**, 388.
[5] Journal of Biological Chemistry, 1921, **47**, 69.
[6] Jour. physiol. et de pathol. gén., 1921, **1**, **19**, 33, abstract International Medical and Surgical Survey, 1921, **2**, 679.
[7] New York Medical Journal, 1921, **114**, 41.

operation in thyroid disease. It is particularly valuable in the group of patients showing dissociated symptoms, for example, in those whose pulses are higher or lower than the metabolic rate would seem to indicate. Mosenthal states that in comparing pulse rates and basal metabolism it appears that there are two types of hyperthyroidism: Type I, in which the pulse rate is 10 or more above the metabolic rate; and Type II, in which it is 10 or more below. Type I responds equally well to roentgen ray or surgery. Type II gives poor results from immediate surgery, doing better with preliminary use of roentgen rays. Diagnostically, the pulse rate is not as reliable as the metabolic rate.

The value of basal metabolism estimations in a goiter clinic is discussed by Frazier and Adler,[1] who consider it of special value in distinguishing cases of true hyperthyroidism from cases of neurasthenia, cardiovascular disease or tuberculosis which present a similar clinical picture, or which may have a concomitant simple adenomatous enlargement of the thyroid. Estimations of basal metabolism help in the elimination of those cases which might be made worse by operation, as well as giving a quantitative, rather than a qualitative index of the thyrotoxicosis.

Among the many other papers dealing with the same subject is one by Means,[2] who notes that metabolism observations are more easily visualized by means of a clinical chart for that purpose. As a clinical chart noting the pulse, temperature and respiration curves is kept in pneumonia or typhoid, so a clinical chart noting the basal metabolism, pulse and body weight is kept in patients with hyperthyroidism. In hypothyroidism, it is possible, on the basis of the information contained on such a chart, to fix the exact dose of thyroid gland necessary to keep a patient's metabolism normal. Such a chart kept in a case of simple obesity due to a disproportion between the food intake and the bodily activity and not to any fundamental change in the combustion in the body, will show a normal metabolism, and the danger of giving thyroid which raises the metabolism in these patients to an abnormal level. The basal metabolism is altered in the blood diseases—leukemias, severe anemias and particularly pernicious anemia.

In discussing the basal metabolism rate in hyperthyroidism, Boothby[3] states that by this method a distinction can be drawn between mild cases of exophthalmic goiter and those conditions known as "effort syndrome," "disordered action of the heart," "cardiac neurosis," "nervous instability," neurocirculatory asthenia" or "neurasthenia," which on superficial examination present some of the signs and symptoms of mild exophthalmic goiter, but in which the basal metabolic rate is normal, and which, on close analysis, can be shown not to be dependent on an excess in the body of the thyroid hormone. The basal metabolic rate is of particular diagnostic value in these cases when they are accompanied, apparently without causal relationship, by a colloid enlargment of the thyroid gland, as so often occurs in the regions of the endemic goiter.

[1] American Journal of the Medical Sciences, 1921, **162**, 10.
[2] Journal of the American Medical Association, 1921, **77**, 347.   [3] Ibid., 252.

The *basal metabolism in fever* is of practical importance to the physician in the calculation of the fever diets. DuBois[1] reviews the literature upon the subject and refers to some unpublished work by himself and his co-workers on the question of metabolism and fever. The paper should be read in full. He states that it is possible to estimate the basal metabolism of a patient by first calculating his normal according to surface area standard. To this we should add about 13 per cent for each degree Centigrade above the normal temperature (7.2 per cent for each degree Fahrenheit). This should be increased by 10 per cent in the case of toxic patients with great destruction of body protein, and by approximately 10 per cent in all other febrile patients who are receiving much food. A further allowance of from 10 to 30 per cent for muscular activity may be necessary if the patients are restless.

The *basal metabolism as an index of operability* is susceptible to considerable error, as pointed out by Plummer in closing the discussion on the whole subject of basal metabolism before the American Medical Association, June, 1921. Plummer states that it is the status of the patient relative to the basal metabolism that is of significance in determining operability. Mayo[2] puts it this way: In a given patient a basal metabolic rate of plus 85 to 100 may fall to plus 35 or 40 if a patient is placed under rest and treatment. This may, however, be but a fictitious improvement. A patient with a metabolic rate of plus 56 who has survived a recent exacerbation and is improving is a safer risk than a patient with a rate of plus 46 who is on the rising wave of an exacerbation. The basal metabolism estimation is, however, the most fundamental measurement of the patient's condition and in a given individual with a normal basal metabolism there is neither hyperthyroidism or hypothyroidism.

Beall[3] studied the basal metabolism in borderline cases in which group signs and symptoms are not clear and the basal metabolism may not be markedly increased. Among 42 patients of the borderline group an increase in the basal metabolism of 10 per cent was present in two-thirds of the cases diagnosed as mild hyperthyroidism. A corresponding increase of 10 per cent was present in one-fourth of those cases in which the clinical signs and symptoms were not considered sufficient to warrant a diagnosis of hyperthyroidism as being the prime factor in the diseased condition. As the basal metabolism rose, the percentage of cases clinically falling into the hyperthyroidism groups increased rapidly.

The basal metabolism, as well as blood-sugar tests, were studied in patients with pulmonary tuberculosis by McBrayer.[4] He concludes that these determinations are of no practical value in the differential diagnosis of chronic pulmonary tuberculosis and hyperthyroidism. Briefly stated, in about one-third of the cases of chronic pulmonary

[1] Journal of the American Medical Association, 1921, **77**, 352.
[2] Medical Record, 1921, **100**, 177.
[3] Journal of the American Medical Association, 1921, **76**, 1639.
[4] Ibid., **77**, 861.

tuberculosis, the basal metabolic rate and the blood-sugar are both increased; in about one-fifth of all such cases there may be an increased basal metabolic rate and a normal blood-sugar, or just the reverse, while in a much smaller percentage of cases you may find any change in either basal metabolic rate or blood-sugar; very seldom, however, would both be decreased or even one decreased and the other normal.

THE HEART IN HYPERTHYROIDISM. Cardiac symptoms are extremely frequent and vary greatly in degree of severity in hyperthyroidism. Goodpasture[1] has studied the myocardial lesions in 2 cases of hyperthyroidism, in both of which auricular fibrillation had been present some time before death. In each instance the cause of death was evidently myocardial exhaustion. In these hearts there was found acute necrosis of the myocardium, in one so extensive as to involve a large part of the left ventricular muscle. In one patient the hyperthyroidism was associated with exophthalmos, in the other without exophthalmos. The thyroid gland in each was hyperplastic. The extent of myocardial necrosis, however, was quite different in the two, being very extensive and diffuse in one, limited and focal in the other. Goodpasture is of the opinion that in these cases the myocardial necrosis was the result of some terminal, and as yet unknown, injury, perhaps an infection or a sudden functional strain, etc.

Goodall[2] states that a large number of cases treated by physicians appeared to get gradual cardiac failure, while a certain number treated by surgeons die suddenly from the same cause. Ventricular fibrillation appears to be the reason why these exophthalmic goiter cases succumb to heart failure after operation, and the conclusion he arrived at from a study of his records was that there were two factors which tended to ventricular fibrillation, one of them a preëxisting myocardial degeneration and the other a high blood pressure. He believed that the blood pressure in exophthalmic goiter was triphasic: First a temporary rise, very transient, then a fall, and then a rise again. After operation, the blood pressure tended to rise, and that rise might be so considerable that the blood pressure at the end of the operation was twice the pressure at the start. If there was a degenerated myocardium and it was suddenly confronted with a high blood pressure, it was reasonable to expect calamity. If the myocardium was degenerated and the blood pressure high, the surgical risk was very great.

The *relation of hyperthyroidism to diabetes mellitus* is discussed by Fitz.[3] Although his observations do not warrant definite conclusions, his studies enable him to draw attention to certain features with regard to the relationship between thyroid disease and diabetes. Hyperthyroidism and diabetes occur together in the same person in a small number of cases. There is no established evidence that such coincidence is more than chance. The diabetes usually follows the thyroid disturbance, but may precede it, and tends to parallel in severity the severity of the thyroid intoxication. There is no reason for assuming

[1] Journal of the American Medical Association, 1921, **76**, 1545.
[2] British Medical Journal, February 19, 1921, 269.
[3] Archives of Internal Medicine, 1921, **27**, 305.

that partial thyroidectomy alone has any curative effect on diabetes, as the patients in Fitz's series with non-toxic goiter who were operated on showed no improvement of the diabetes. Certain patients with toxic thyroid disease and diabetes, on the other hand, improve to a considerable degree after the thyroid symptoms are checked. This probably occurs because of a change in the rate of metabolism and not because a portion of the thyroid gland has been made functionless. Before this supposition can be established, more accurate information must be obtained with regard to the effect of an increased rate of total metabolism from thyroid intoxication on the carbohydrate metabolism of diabetes.

Hypothyroidism. Sporadic cretinism (*infantile myxedema*). Goldstein[1] reports the cases of 4 Jewish girls who showed cretinoid symptoms and improved under thyroid treatment. Block[2] reports the after medical history of 3 girls brought to the Long Island College Hospital fourteen years ago. These girls were then ten, eleven, and twelve years old, respectively, about three feet in height and apparently abnormal mentally. A diagnosis of hypothyroidism was made and treatment by thyroid extracts begun. The therapy has been continued until the present time. One of the sisters is now five feet tall and weighs 110 pounds. She seems mentally about normal and has charge of an entire manicure department in a large store. The other sisters are five feet two inches in height, and both appear normal mentally. One is married and has an apparently healthy child of two years. For fourteen years these girls have been taking thyroid extract, at times as much as 50 gr. a day. At present each takes 5 gr. a day and each third day the dosage is being cut 1 gr. This family group is reported to show the typical familial endocrinologic disturbance, and to prove that properly handled cases of mental disorder can apparently be cured. This instance also demonstrates that, if intelligently used, thyroid can be taken for many years without apparent harm to the patient.

The *differential diagnosis between rudimentary myxedema and hypoovarianism* is discussed by Kuhlmann.[3] He contrasts two cases that resemble each other clinically in certain features of myxedema. They were different as to etiology, however, one being due to hypothyroidism and the other to hypoövarianism. The following case histories[4] are given.

The first case was that of a woman who took sick during her menopause. The thyroid was not palpable and her hair was falling. The facial expression was not characteristic and there was sagging of the parotid region. The skin was atrophic. She improved under thyroidin treatment. The diagnosis of myxedema was substantiated at autopsy by excessive connective tissue and lack of colloid substance in the thyroid. The diagnosis was somewhat clouded by a septic fever due to an infection of the kidney pelvis.

[1] Journal of Medical Society, New Jersey, 1921, **18**, 184.
[2] Long Island Medical Journal, 1921, **14**, 280.
[3] München. med. Wchnschr., 1921, **68**, 550.
[4] International Medical and Surgical Survey, 1921, **2**, 701.

The second case suggested a diagnosis of myxedema by the dry and thick skin: The skin of the extremities resembled that in scleroderma. The psychical condition was that of myxedema. The hair was falling out. This case differed from the other in that it began at puberty; the menses were absent, due to hypoplasia of the genitals. Thyroidin had no effect, although the thyroid was not palpable. Myxedema was excluded. Evidences of chlorosis were absent. The interstitial ovarian gland was probably affected, as shown by absence of libido. After ovarian transplantation the facial expression improved and also the psychical reactions. Menstruation had not yet appeared at the time of the report.

Treatment of Exophthalmic Goiter. Belot[1] concludes that radiotherapy is the best of all treatments for exophthalmic goiter and gives surprisingly good results if started early. In 45 cases, 20 per cent were partially improved, 70 per cent with definite and prolonged improvement, 5 per cent not improved, among those who completed the course. He states that operative treatment should not be considered until after the failure of radiotherapy. Radiotherapy has also been found useful in the experience of Gaarenstroom.[2] On the other hand, Schulte,[3] another foreign writer, is opposed to the use of the roentgen ray. He says that it renders operative measures more difficult if they finally have to be applied, and that fatalities have been reported, as also the transformation of an exophthalmic goiter into myxedema. He ascribes the success with operative measures in America in large part to the fact that people here are more accustomed to operations in the early stages of disease.

Litchfield,[4] of Pittsburgh, is an ardent advocate of roentgen therapy before surgery is resorted to, and he believes that cases that are cured by the roentgen-ray treatment are just as well cured as those that have been cured by surgical operation, and that inasmuch as the roentgen ray cure is a matter of repeated application, with considerable intervals between them extending over a period of months—possibly a year or more—there would seem to be much less danger of reducing the thyroid gland more than necessary. He has at the present time seven cases under roentgen-ray treatment, and all are improving. Utley[5] contends that while in the hands of a skilled radiographer it is unquestionably a valuable therapeutic agent, in the hands of many men who are using the roentgen ray throughout the country it is apparently dangerous.

Foss[6] exemplifies the attitude of those who advocate surgical treatment. He says with regard to these patients, when cared for by competent surgeons in competent hospitals, that nothing in surgery is more

[1] Bulletin Medical, 1920, **34**, 1063; abstract, Journal of the American Medical Association, 1921, **76**, 620.
[2] Nederlandsch Tijdschrift v. Geneeskunde, 1921, **2**, 209; abstract, Journal of the American Medical Association, 1921, **77**, 1060.
[3] Ibid., **1**, 1243; abstract; Journal of the American Medical Association, 1921, **76**, 1622.
[4] Pennsylvania Medical Journal, May, 1921, 547.
[5] Ibid., 544.   [6] Ibid., October, 1921, 35.

brilliant and satisfactory, and, as applied to this disease, the favorable results are more definite, more immediate and more lasting than from any other form of treatment. Herman-Johnson[1] states that roentgen-ray treatment should be regarded not as a rival but as an adjuvant to surgery, and, except insofar as its early employment tends to reduce the number of cases coming up for surgical consideration, its use need not affect the question as to when an operation becomes advisable. The benefit derived from roentgen-ray treatment is usually very pronounced, pulse rate and sweating diminishing, and definite improvement taking place. Usually, the applications are over the thyroid, though some observers apply the rays over the thymus and over the sympathetic in the neck, the good effects appearing to be constitutional as well as local. It is best to commence with small frequent doses, combined with rest in bed when practicable, and the treatment should be given a trial even in apparently hopeless cases.

In the discussion[2] of this subject before the Clinical Section of the Royal Society of Medicine, there again was evident difference of opinion, *e. g.*, Mr. Walton spoke of the good results of surgery where medical treatment had failed. His opinion of roentgen-ray treatment was unfavorable. He advocated medical treatment (1) if the symptoms had been in evidence for less than six months; (2) as a preliminary to surgical treatment; (3) before a second operation in a case of relapse, where there was an enlargement of the remaining portion of the thyroid after operation. On the other hand, Stoney gave particulars of some 200 cases which she had treated by roentgen rays during the last thirteen years. Of these, 78 were quite cured and strong after a long interval since cessation of treatment, 66 were much better, 28 were no better; many of the others had been lost sight of. Roentgen-ray treatment should only be entrusted to a first-class radiologist. If time were of vital importance in any case, surgery might offer the greater advantage; in all other cases, roentgen rays should be preferred, since they spared the patient the mental upset of operation, sometimes repeated, as well as the pain and risk to life. The disadvantages of roentgen rays were the tediousness of treatment—largely obviated by taking the disease in hand early—and the occurrence of telangiectasis and scars, both of which, however, occurred less and less frequently with improvement in technic.

Mayo[3] states that at Rochester 25,000 thyroids have been operated upon or treated medically when operative procedure was inadvisable. The roentgen ray has produced severe scarring and is dangerous in that it may produce a complete destruction of the gland. The earlier the operation, the less the risk. Mayo states that recently as many as 146 operations have been performed between deaths. Under the unfavorable conditions of late operation, the mortality has been from 15 to 20 per cent. He states that patients with exophthalmic goiter pass through exacerbations of symptoms which are largely influenced by psychic

[1] Archives Radiology and Electrotherapy, June 1921.
[2] British Medical Journal, 1921, **1**, 268, 342 and 425.
[3] Medical Record, 1921, **100**, 177.

stimuli, and are easily exhausted. At this period, the patient should be treated medically and not surgically. A patient with a metabolic rate of plus 56, who has survived a recent exacerbation and is improving, is a safer risk than a patient with a metabolism rate of plus 46 who is on the rising wave of an exacerbation. During a period of exacerbation, ligation, hot-water injections, and roentgen-ray treatment may be given, if necessary, in conjuction with absolute rest.

In discussing surgery *versus* the roentgen ray in the treatment of hyperthyroidism, Crile[1] states that from a study of the evidence offered by those who advocate roentgen therapy, and a consideration of his own experience, he is inclined to believe that the surgical treatment of hyperthyroidism, combined with physiologic rest, yields the most favorable results.

The RELATION OF THE THYROID TO PREGNANCY was discussed by Fruhinsholz and Parisot[2] who state that normal gestation is accompanied by a state of physiological hyperthyroidism which is compensatory and is most manifest during the last months. In certain rare cases this hyperthyroidism may at any stage of gestation become pathologically increased. A preëxisting state of hyperthyroidism is not conductive to a high degree of fecundity. It is exceptional for the onset of pregnancy to lead to an aggravation of a preëxisting state of hyperthyroidism. Hypothyroidism is even less favorable than hyperthyroidism to the occurrence of conception, but, if conception occurs, the influence of the gestation on the hypothyroidism may be favorable, aggravating, or indifferent. A latent insufficiency of parathyroid function may be revealed during the course of pregnancy by the occurrence of tetany. Pregnancy supervening in patients who are the subjects of hyperthyroidism or hypothyroidism almost invariably takes a normal course, and such complications as occur are of toxemic nature. The thyroid hypertrophy of pregnancy may be followed after delivery by athyroidism.

Malignant Tumors of the Thyroid. Our knowledge of the incidence of malignant tumors of the thyroid is very meagre for lack of accurate data. Wilson[3] states that the number detailed in the literature to date is probably not more than 1000. Only 34 have been reported by American authors. That thyroid tumors are undoubtedly more common than these statistics would indicate, is evidenced by the fact that Wilson received personal communications from 67 American surgeons reporting 167 cases which had not appeared in the literature; in other words, five times as many cases have been met with in the experience of a small group of American surgeons as have appeared in the entire literature from all American sources. The incidence of malignant tumors among thyroid cases is exemplified by the experience of the Mayo Clinic up to January 1, 1921. In this clinic, among 10,682

[1] Journal of the American Medical Association, 1921, 77, 1324.
[2] Gynéc. et Obstet., 1921, 4, 4; abstract, British Medical Journal, November 19, 1921, Epitome, p. 76.
[3] Annals of Surgery, 1921, 74, 129, and Surgical Clinics of North America, 1921, 1, 1291.

simple goiters and 5876 exophthalmic goiters which had been operated upon, 207 were malignant. Beside these 207, there were 83 cases in which the diagnosis of malignancy was made, but which were inoperable. The age incidence was greatest in the fourth, fifth and sixth decade. Sixty-nine per cent occurred in women, and 31 per cent in men. Patients usually seek medical advice because of recent rapid growth in a long-standing nodular tumor of the thyroid. Some give histories of slow, continuous growth. Wilson discusses the clinical manifestations and course of the disease as follows:

Of the total number of patients examined in the Mayo Clinic about one-fourth had noticed symptoms of continuous growth for one year or less, and about one-third had noticed symptoms of continuous growth for ten years or more. It may be doubted whether the process in the latter was malignant from the beginning of the continuous period of growth. Of the patients whose conditions were considered inoperable at the time of their first examination in the Clinic, more than one-half had noticed symptoms which might be interpreted as indicative of the presence of malignant tumor for one year or less, while one-fourth of them had noticed similar symptoms which had existed for ten years or more. Thus it will be seen that while a sudden increase in rate of growth of a long-standing nodular tumor of the thyroid in a patient more than thirty-five is strongly indicative of beginning malignancy, a slow, continuous growth may be almost equally indicative of the same condition. The distinction is important because, in much of the older literature, the impression is given that the rate of growth is almost always very rapid.

The surface of a malignant thyroid is more apt to be irregular and nodular than when the enlargement is due to inflammation. The irregular nodules are readily palpable. They are, however, not more regular or nodular at the beginning than are non-malignant adenomas.

Accompanying the thyroid enlargement, and due to it, are symptoms of pressure on the larynx, trachea, esophagus, and neighboring nerve trunks. The voice may change, usually deepening. There may be coughing and excess of mucus from the trachea. Even early there may be difficulty in swallowing. Pain in the region of the thyroid, in the neck generally, and extending behind the ears and outward to the shoulders may be an early symptom. There are likely to be cardio-vascular disturbances, such as arrhythmias, palpitation, and pain resembling angina pectoris. At this early period, the patient's general health may be good, and he may continue his usual vocation until the disease is well advanced before seeking medical advice.

As the disease progresses, all the symptoms become aggravated. The pain may become more constant and neuralgic in character. As infiltration of the surrounding tissues occurs, the patient complains of "drawing" pains in the gland, which is also tender on pressure. The trachea is often infiltrated, although sometimes only displaced. Invasion of the trachea interferes with its blood supply, causing edema and dyspnea. Intratracheal hemorrhage may develop early. Interference with respiration may become serious; the patient sleeps in a sitting

posture. The pressure on the esophagus may cause dysphagia. Difficulty in swallowing is probably due at first to spasm, but later to direct pressure. Later, the tumor may become large, hard and immovable. The pressure from it causes the veins of the neck and arms to stand out prominently. The skin over the tumor becomes red and adherent to it. The patient loses weight and strength rapidly. Cachexia is not nearly so common as in cases of tumors of the alimentary canal, for example, being noted in perhaps not more than one-fifth of all fatal cases. Metastatic deposits are most frequent in the lungs. The skull, brain, and liver are also frequent sites. A few cases have been reported of malignant tumors of thyroid tissue in organs distant from the thyroid in which necropsy revealed no evidence of malignancy in the thyroid itself.

An interesting example of a TUMOR COMPOSED OF ECTOPIC THYROID tissue is reported by Whale.[1] A woman was admitted to the hospital. The existence of slight pyrexia and a suspicious fulness in the neck suggested the possibility of perforation into the cervical fascia, with the dread sequela of infective mediastinitis. An endoscopic examination was made and, at the level of the second dorsal vertebra, a tumor was discovered, attached to the midline of the dorsal surface of the esophageal lining. The protuberance was paler than the surrounding mucosa. In size it was smaller than a cherry but much larger than a pea and attached by a broad pedicle. It was removed in entirety and histologic study revealed the thyroid tissue of which it was composed.

PARATHYROID GLANDS.

An excellent review of the literature with a comprehensive bibliography is to be found in Boothby's[2] article on the parathyroid glands. He traces the development of our knowledge from the time of the first anatomic and physiologic studies to the present. He summarizes our present knowledge of the function of the thyroid glands as follows:

1. In many species of animals the removal of all parathyroid tissue causes death from tetany, within a few days in most instances; the herbivora are less liable to tetany than the carnivora; age appears to have a definite influence on its frequency and severity, as probably also do pregnancy and lactation. There is some evidence of late trophic changes in those animals that survive parathyroidectomy and have few or no tetanic symptoms.

2. The preservation of very small amounts of parathyroid tissue prevents or renders the tetany less intense.

3. From the evidence at hand, the function of the parathyroids appears to be distinct and separate from that of the thyroid; their only relationship seems to be anatomic and not functional; the parathyroids are not embryonic thyroid tissue.

4. There is evidence that their function is in some way concerned with calcium or guanidin metabolism or with both; they may play

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[1] Lancet, 1921, **2**, 987.   [2] Endocrinology, 1921, **5**, 403.

some part in the regulation or maintenance of the acid-base equilibrium in the body.

5. The experimental evidence pointing to the parathyroids as the primary cause of idiopathic tetany, unassociated with operative procedures on the thyroid, is very limited.

6. The only definite clinical entity which has yet been proved experimentally to be of parathyroid origin is the tetany occasionally seen after operations on the thyroid. In these conditions calcium in large doses usually ameliorates the symptoms. The reports as to the benefit obtained by parathyroid transplantation or feeding are not convincing.

Klein[1] reports the instance of a girl, aged eighteen years, who, following an operation for goiter, developed some evidences of myxedema and tetany. Under calcium therapy, the tetany subsided. Comby's[2] clinical observations would indicate that an acquired idiocy of parathyroid origin is not uncommon. The apathy, tremor, and convulsions associated with parathyroid idiocy, as observed clinically, recalls the clinical picture of parathyroidectomy in animals. Parathyroid treatment is followed by striking improvement.

The effect of parathyroidectomy was studied by Hastings and Murray.[3] The previously observed calcium deficiency in parathyroidectomized dogs was verified, but no support is found for theories based on a disturbed acid-base equilibrium. Underhill and Nellans,[4] however, repeating former experiments, come to the conclusions that there is a lowered blood-sugar content following operation and, while a little or no change in the carbon dioxide capacity occurs up to the onset of tetany, after this period there is a decided tendency toward a diminished alkali reserve.

THE PITUITARY GLAND.

Diabetes Insipidus. Cushing,[5] in an article on disorders of the pituitary gland, calls attention to the error in our past conception of the diuretic action of the posterior lobe extracts. Until Motzfeldt's studies, which showed that these extracts were really antidiuretic in action, it was difficult to understand why diabetes insipidus was so often an accompaniment of pituitary insufficiency rather than of its counter-state. This observation gave us for the first time a rational basis for the treatment of the disorder, but, unhappily, posterior lobe extracts appear to be ineffective when given by mouth, as so many glandular extracts are, and there are limits to daily hypodermic injections of a substance such as pituitary extract. Brunn[6] found that the injection of pituitary extract in normal individuals with normal kidneys caused the secretion of a highly concentrated urine. With diseased kidneys, the specific gravity does not increase after the injection, even when there is restriction of the intake of fluids. In diabetes insipidus, according to the

[1] Deutsches Archiv. für klinische Medizin, 1921, **135**, 161.
[2] Archives de Médecine, 1921, **24**, 303.
[3] Journal of Biological Chemistry, 1921, **46**, 233.
[4] Ibid., **48**, 557.
[5] Journal of the American Medical Association, 1921, **76**, 1721.
[6] Medizinische Klinik, 1921, **17**, 871.

studies of Meyer and Meyer-Bisch[1] who made tests in a young woman with salt retention, there is a marked effect of pituitary extract (posterior lobe) on the exchange of salt and water between the blood and tissues and between the blood and the urine. The findings were confirmed by experiments on dogs. The sodium chloride content of the blood subsided to normal under its influence, while the percentage in the urine doubled, and the output of urine declined. The results show that pituitary extract acts on the tissues as well as on the kidneys. In a case of pure polydipsia, no effect from the pituitary extract could be detected, and there was no concentration of the urine—as occurs in true diabetes insipidus—during days of restriction of intake of fluid. Schulmann[2] states that pituitary polyuria in contrast to other forms, is not associated with the retention of certain urinary elements. The only abnormality is the flood of water. Schulmann and Desoutter[3] state that while extract of the posterior lobe of the pituitary is unquestionably the most effectual treatment at our command to date, it probably does not definitely modify the prognosis of diabetes insipidus. It does, however, reduce or abolish the two most distressing features of the disease, the tormenting thirst and the indefinable malaise which prevents sleep. Pituitary treatment may likewise act on other manifestations of secretory insufficiency, and it may sometimes be usefully reinforced with thyroid or suprarenal extract. In Amat's[4] patient the ocular manifestations due to pressure on the optic chiasm displayed marked improvement under pituitary treatment, while the urine output dropped from 8 to 4 liters per day. Gorke and Deloch[5] reported marked improvement in three cases with gastro-intestinal disturbances associated with diabetes insipidus, under pituitary treatment.

Hereditary diabetes insipidus is reported by Jansen and Broekman[6] who found 14 cases of diabetes insipidus in five generations, except in the second, in which apparently no member was affected. Four of the cases were males and 10 females. This is contrary to the general rule that hereditary diabetes insipidus is commonest in the male. They allude to the pedigree complied by Weil of five generations consisting of 220 persons, of whom 35 (21 men and 14 women) had diabetes insipidus. They have also collected 11 other reported cases of hereditary diabetes insipidus. As in the cases reported by Weil, who refer to hereditary diabetes insipidus as a "healthy disease," the patients of Jansen and Broekman were able to follow their occupation, felt quite well and reached old age. The symptoms usually developed in infancy, sometimes later, became more marked about the twenty-fifth year, and then diminished. The abundant excretion of water had no effect upon the heart. The blood-pressure was normal. Weil maintained that

[1] Deutsches Archiv für klinische Medizin, 1921, **137**, 225; abstract, Journal of the American Medical Association, 1921, **77**, 1293.
[2] Médecine, Paris, 1921, **2**, 799.
[3] Abstract, Journal of the American Medical Association, 1921, **76**, 688.
[4] Siglo Médico, 1921, **68**, 720.
[5] Medizinische Klinik, 1921, **17**, 1140.
[6] Nederl. Tijdschr. v. Geneesk., May 7, 1921; abstract, British Medical Journal August 20, 1921, 25.

the hereditary form of diabetes insipidus should be separated from the acquired form, but the present writers hold that there are no distinguishing features except heredity. Weil suggests that there is a difference in prognosis, but, as the writers point out, in many cases of diabetes insipidus in which cerebral tumor, cerebral syphilis, tuberculous meningitis, etc., can be excluded, the prognosis is also favorable.

Evans and Wallis[1] report 2 cases of diabetes insipidus which presented, in addition, intermittent glycosuria. They do not consider the glycosuria an evidence of diabetes mellitus, on account of its slight degree, its intermittent nature, its non-progressive course, and its independence of diet. In neither case did a large carbohydrate meal lead to the appearance of sugar in the urine. The intermittent nature of the glycosuria distinguishes the cases from diabetes innocens. The only group of cases to which their cases bear any resemblance are the intermittent glycosurias observed in acromegaly. There was found a lower sugar tolerance than normal in both cases, and a lowered renal threshhold in 1 case. In the present state of our knowledge, such a glycosuria is to be regarded as an indication of a polyglandular dystrophy, and not necessarily as a sign of pancreatic disease. The association of pancreatic disorder with acromegaly is referred to by several writers, but in the patients of Evans and Wallis there was no evidence of pancreatic disease other than the glycosuria; the diastase reaction was normal in both.

HYPOPITUITARISM. Apart from the occurrence of diabetes insipidus where there is evidence of hypopituitarism there occurs the Froelich syndrome. Kay[2] reports one of the youngest cases on record. A full-term baby started to gain weight rapidly at the third month. At the same time, mentality retrogressed. Somnolence was almost continuous, and marked polyuria became evident. Treatment at first by thyroid gland and subsequently with pituitary gland resulted in marked improvement.

An unusual hypophysial syndrome is reported by Friedman.[3] A male of nineteen presented dwarfism and obesity of nine years' duration, hypertension, recurrent pains in the region of the spine for six months. Nine years ago the patient began to grow stout. He gained much weight in two months. Since then there had been very little growth in height. His abdomen became pendulous, his fingers stubby, feet remained small and face became ruddy. His speech became somewhat hesitant. He had some impairment of memory. He had dimness of vision for the last two months and occasional headaches. Nocturia was present, but no polydipsia. The mammæ were well developed and the fat distribution was of the feminine type. There was an overgrowth of hair at the bridge of the nose, and the body was covered with fine lanugo hairs. The genitals were small.

The *relationship between the hypophysis and the sexual organs* is frequently noted in diseases involving the former. Peritz[4] states that

[1] Lancet, 1921, **200**, 70. [2] Endocrinology, 1921, **5**, 325.
[3] New York Medical Journal, 1921, **114**, 113.
[4] Ztschr. f. Urol., 1921, **15**, 207.

the relationships between the hypophysis and the puberty gland are reciprocal—gigantism is associated with a mental infantilism. The hypophysis has an inhibitory effect upon the function of the puberty gland, and *vice versa*, as soon as the sexual glands function the body ceases to grow, body growth being controlled by the hypophysis. If both glands remain undeveloped, the hypophysial dwarf results, with stunted growth and infantile mind, showing the effect of the puberty gland upon the nervous system. Whether dwarfism is secondary to the genital gland disturbance, or is due to a pluriglandular disease, is immaterial, although the latter theory is more acceptable. Two dwarfs markedly increased in size after administration of hypophysial extract without corresponding development of the puberty gland. The dystrophy of the hypophysis was caused by a hydrocephalus of the type seen in congenital lues, not characterized by cephalic enlargement.

Pituitary Headache. Redwood[1] and Hodges[2] discuss headaches of pituitary origin. Redwood's experience concerns 11 patients in whom all factors in the production of headache could be eliminated except the pituitary. Some of these patients had associated pituitary disturbances, such as diabetes insipidus. Seven had very small sellas, closed in by the clinoids, and 4 had sellas normal in size, but the clinoids enclosed the fossa. Six had headache every day, 3 every two or three days and 2 once a month. One patient had been troubled with headache since he could remember; the other patients from six months to seven years. As the result of pituitary treatment, in 8 cases the headache disappeared entirely or was greatly relieved; 2 cases of long standing, were not benefited in the slightest, and 1 patient has not been heard from in several months. Hodges contrasts migrainous and pituitary headaches. Migrainous headaches occur paroxysmally in neurotic individuals, often with a history of direct heredity, and at any time of life, and are congestive in type, and characterized by periodic attacks of pain, continuing for variable periods in the course of the fifth nerve, and often associated with nausea or vomiting and various vasomotor disturbances, which are intractable to treatment. Pituitary headaches are localized and persistent in type ,and occur in patients often showing clinical dyspituitary disorders, and are usually relieved by continuous and proper glandular feeding. The prognosis in migrainous headaches is uncertain and discouraging, and generally irresponsive to any treatment before a patient is forty years of age. After approximately that age, there may be improvement or, sometimes, spontaneous recovery, while in pituitary headache, the prognosis is favorable and satisfactory, if treated early by appropriate glandular extract.

The Pituitary and Wood Alcohol Poisoning. Ziegler[3] is of the opinion that a profound injury of the pituitary body is the fundamental lesion in all cases of methylic poisoning. The acute toxic symptoms are typical of such a lesion, while the chronic symptoms are equally sig-

[1] Virginia Medical Monthly, 1921, **48**, 25.
[2] Ibid., 1921, **48**, 203.
[3] Pennsylvania Medical Journal, 1921, **25**, 177.

nificant. The changing but steadily contracting fields, the fugitive scotomata, the visual loss and recovery, the sclerosed or atrophic nerve heads, the fixed and dilated pupils, the temporary paresis of the extra-ocular muscles, the ptosis, the ataxic gait and the mental hebetude are all characteristic of pituitary involvement.

Gigantism. A giant 7 feet 8 inches is reported by Robinson[1] with no symptoms of intracranial pressure and with an roentgen-ray finding of a pituitary fossa quite normal in shape. He possessed average intelligence and the sex organs were quite normal. The experimental production of giantism is reported by Uhlenhuth[2] who was able, by feeding anterior pituitary to salamanders, to increase their size to the greatest known for the species. Feeding of the anterior lobe caused not only a marked acceleration of growth, but a continuation of the growth beyond the average size of the species, thus resulting in gigantism. The continuation of growth beyond the normal size of the species is not due to an increased amount of food, and it would seem that at a stage where growth ceases or is greatly diminished under normal conditions, cell proliferation can be actually enforced by the specific growth-promoting substance contained in the anterior lobe of the hypophysis.

GIGANTISM WITH HEMORRHAGIC OSTEOMYELITIS of a metacarpal bone occurred in the patient reported by Packard and Barrie.[3] The writers believe that although absolute proof of the direct association of hemorrhagic osteomyelitis and a disturbance of the anterior pituitary is lacking, there is a greater probability of such an association than a mere coincidence. The hemorrhagic process in the bone is regarded as an evidence of reparative effort in the bone in which there is a disturbance of the nutrition brought about by pituitary disturbance.

Dwarfism, from clinical studies, would seem to be related to hypopituitarism occurring early in life. Clinically, the 4 cases reported by Brandis[4] would seem to support such an opinion. Treatment, however, with pituitary extract failed to produce any benefit. Marañon and Solanilla[5] report an instance of dwarfism associated with the pituitary adiposogenital syndrome.

Cholesteatomatous Cystic Tumor of the Pituitary Gland. Under this head, Lockwood[6] reports a case of a Polish laborer, aged twenty-five years, who, seven years prior to coming under observation, began to lose vision in the temporal field of his left eye. This was followed by some headache, bitemporal hemianopsia and optic atrophy, with loss of hair and change of skin texture, loss of sexual power and atrophy of the genitals, some redistribution of fat, and a subnormal temperature, slow pulse and low blood-pressure. The positive laboratory findings revealed an increased sugar tolerance, a negative epinephrin test, a gastric hypoacidity and roentgen-ray findings of an enormously enlarged sella turcica. The roentgen-ray treatment and whole pituitary

[1] British Medical Journal, 1921, **1**, 560.
[2] Journal General Physiology, 1921, **3**, 347.
[3] Journal of the American Medical Association, 1922, **78**, 8.
[4] Deutsches Archiv für klinische Medizin, 1921, **136**, 323.
[5] Abstract, Journal of the American Medical Association, 1921, **77**, 1929.
[6] Journal of the American Medical Association, 1921, **76**, 1218.

by mouth caused temporary improvement. Shortly afterward, however, the patient went into delirium and died. Necropsy revealed a cystic tumor the size of a pigeon's egg involving the pituitary gland and extending anteriorly and laterally. The sella turcica measured $1\frac{1}{2}$ inches laterally by 2 inches antero-posteriorly. It was markedly enlarged and hollowed out, with erosion of bone. The tumor itself measured 2 by $1\frac{1}{2}$ inches and consisted of one large cyst with numerous smaller cysts at the posterior end. The tumor did not involve the brain tissue, but it had forced the cerebral peduncles widely apart. At the base of the tumor there was pituitary tissue about the size of a cherry pit and showing evidence of adenomatous changes. Microscopic examination revealed cholesteatomatous cysts of the hypophysis with hyperplasia (compensatory) of the parenchyma cells. As Lockwood points out, the futility of the use of the roentgen ray is evident unless it can be definitely shown that the tumor is an adenoma. Operative procedure is the method to be chosen for attacking such conditions as presented by his patient.

The **Relation of Acromegaly to Thyroid Disease** was made the subject of a statistical study by Anders and Jameson.[1] These writers refer to the observation of Berkeley that the anterior lobe of the hypophysis is abundantly supplied with sympathetic fibers while the posterior lobe is devoid of such fibers, which clarifies our conception of the interrelation between diseases of the former and hyper- and hypothyroidism. Anders and Jameson collected 215 cases of acromegaly among which lesions of the pituitary were mentioned in 99 instances, and lesions of the thyroid in 68 instances, or in other words, a disturbance of the thyroid function in 33 per cent of the cases of acromegaly. These authors state that it is highly probably that in many instances of pituitary disease with its usual syndrome, the coexistence of thyroid alterations and symptoms resulting therefrom are overlooked, as was true of 1 of their 2 cases. Their investigations indicate that hypothyroidism is more commonly associated with acromegaly than hyperthyroidism, and that those combined cases which manifest myxedematous features are decidedly improved as the result of the use of thyroid preparations.

It follows that the recognition of the indications of hypothyroidism in connection with acromegaly is a matter of the utmost importance. In cases of acromegaly in which merely suspicious features of either hypo- or hyperthyroidism exist, it is strongly urged that the metabolic rate be determined. The approved sugar tolerance test should be carried out in all cases of acromegaly with a view of determining the state of both the pituitary and the thyroid function. Nothing of special significance bearing upon the etiological factors of the disease under consideration resulted from their studies with the possible exception of the facts developed in connection with the age groups by decades. These revealed that the great majority of cases of acromegaly with thyroid disturbance arise between the thirtieth and fiftieth years of age, and that both during the decade prior to that period of life and sub-

[1] American Journal of the Medical Sciences, 1922, **163**, 190.

sequently the cases are far less numerous than in acromegaly without thyroid disturbance. Again, it should be noted that in the cases of acromegaly in which thyroid disturbance is combined, the latter usually arises a number of years after the onset of the former, *i. e.*, when the stage of hypopituitarism is reached.

The Relation of the Pituitary to Epilepsy was studied by Lowenstein[1] in a series of 16 cases selected without regard to any presupposed pituitary factor. Five cases displayed one or more features suggesting pituitary disturbance. In 8 cases sella changes could be demonstrated. Two patients showed abnormalities of the visual fields, 1 of whom showed bilateral temporal defect. In 5 cases, or 31 per cent, benefit followed the administration of pituitary gland. Lowenstein states that the preferable product seems to be the whole gland and the most satisfactory mode of treatment is hypodermically. No cases showing the "typical epileptic constitution" were benefited. There was no improvement in those patients with abnormalities of the fundi or visual fields. Neither physical signs referable to the pituitary, mental reactions (except the "typical epileptic constitution"), changes in the sella turcica demonstrable by the roentgen ray or variations in weight or health offered any criteria by which the relative degree of success or failure of the treatment could be predicted.

Clark[2] calls attention to the occurrence of relatively benign fainting attacks in growing adolescents which simulate minor epilepsy. They are to be differentiated from this latter condition by the absence of the epileptic character and the general physical and mental stigma of the grave disorder. The syncopal states are but a part of the obscure clinical picture of dispituitarism. Coincident with the fainting attacks may be low blood-pressure, slow pulse, vasomotor ataxia and a host of defective muscular and skeletal displacements. In the psychical sphere one encounters not infrequently character delinquencies and slow mental development. The line of corrective treatment is physical plus specific glandular therapy. Mild cases recover of their own accord by gradually restoring the glandular and physical balance, but they can be materially helped by proper direction and rest. In many cases of dispituitarism such as Clark outlined, the pituitary gland itself compensates by causing bony erosion and enlargement of the sella for the proper functioning of this gland. This fact has been demonstrated by Timme by the roentgen ray. In his own cases, Clark found the roentgen-ray examinations uncertain of exact determination of this fact.

From the evidence of this paper, one gains the fact that even in the large group of essential epilepsies and the psychoneuroses in which endocrine dysfunctions are present one must not charge too surely the dysfunction as the real cause, but only as a contributing factor in the production of the nervous disorder. There are many other precipitants of the disease in evidence which are much more nearly related to the psychic disorder than the circumstance of an endocrine disturbance.

[1] American Journal of the Medical Sciences, 1922, **163**, 120.
[2] Ibid., 211.

Clark states that by assuming this conservative position our special glandular therapy will not be too heavily charged with remissness when its administration solely results in failure. No two disorders existent in the same individual are essentially in the relationship of cause and effect.

THE SUPRARENALS.

The **White Adrenal Line** is a sign of hypoadrenia, according to Sergent who originally described it. It will be recalled that this line is produced by a gentle stroking of the exposed skin of the abdomen with a blunt object, such as the back of a finger nail or the end of a pencil. In about ten seconds a pure white band appears and lasts from three to fifteen, or more, minutes. Kay and Brock[1] became interested in this phenomenon by its appearance in a case of dystrophia adiposogenitalis. In their patient the injection of adrenalin subcutaneously caused the line to disappear promptly and then quickly reappear, although the other effects of the injection, such as tremor, palpitation, increased pulse and blood-pressure persisted for some hours. Kay and Brock were led to investigate further the phenomenon in some 255 cases comprising all types of disease and a series of normals. A white line was obtained in 58 per cent; a red line (tâche cérébrale) in 9 per cent; an indifferent type of line in 33 per cent. The latter is a deepening of the normal skin tint, with a whitish or reddish admixture, or a red quickly followed by a white band. From their study, Kay and Brock conclude that Sergent's line is a local vasomotor reflex resident in the skin and bears no direct relationship to suprarenal gland activity. The reasons given are: (*a*) Its independence of blood pressure, acute fatigue and other signs of hypoadrenia; (*b*) its frequent occurrence in normals and in a variety of diseases unassociated with hypoadrenia; (*c*) its reappearance in the face of persistent general manifestations of adrenalin subcutaneously administered; (*d*) its peculiar association with scarlet fever. It would appear that the state of the vasomotor system which allows of its best exhibition is found in young adults of either sex, and especially in the exanthem of scarlet fever.

Suprarenal Virilism is a term which has recently found its way into medical literature to describe the association of precocious development of the genitals and hirsutism with suprarenal cortex lesions. This condition first convincingly established by Bullock and Sequeira,[2] in 1905, is discussed in an interesting editorial.[3] The term *virilism*, applied to women, is used in the sense of *masculinism*, in which the sexual characteristics approach those of the male. Thus, in a well-marked example, such as seen with cortical hypernephroma, hirsuties with the distribution characteristic of the male, hypertrophy of the clitoris, atrophy of the mammæ, a manly voice and obesity, or (in boys) muscular development, are present. But there is much variation in the degree of these manifestations. It is obviously influenced by the age of onset;

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[1] American Journal of the Medical Sciences, 1921, **161**, 555.
[2] Transactions of the Pathological Society of London, 1905, **56**, 189.
[3] British Medical Journal, October 1, 1921, 533.

thus, when the change commences in fetal life and both adrenals show hyperplasia, there is feminine hermaphroditism, the internal genital organs being female and the external approaching those of the male; whereas when a cortical hypernephroma starts after birth and is unilateral, the manifestations are less pronounced.

This editorial quotes Glynn who has collected 17 cases, verified by necropsy, in girls showing precocious growth, hirsuties usually of the male type, often obesity and hypertrophied clitoris, between the ages of one and eleven years, most being between the ages of three and seven. Glynn also refers to 4 cases in boys with corresponding changes, except that in some there was remarkable muscular development (Parkes Weber's infant Hercules type). When the onset occurs after puberty, the main features are amenorrhea, sexual disorders, hirsuties and obesity. In Holmes's remarkable case, a girl, formerly normal, developed suprarenal virilism at the age of twenty, and at twenty-four, after removal of a hypernephroma, became normal again. The *British Medical Journal* editorial points out, further, that although suprarenal virilism is the best recognized form, it is by no means the only one and it is possible that the mechanism by which cortical hypernephromas produce these striking changes is indirect; it may be that adrenal over-activity influences the genital glands, particularly their interstitial cells, thus leading to the somatic alterations. Disturbance of the balance between the various endocrine glands must, therefore, be taken into account in considering the etiology of virilism. A few cases of virilism have been reported in association with pineal tumors (nearly all in boys between the ages of four and eight years), and here the contrast to Frölich's adipose-genital syndrome due to hypopituitarism will be obvious, just as virilism as a whole forms a contrast to feminism and infantilism. In very rare instances virilism has been described with ovarian cysts and solid tumors, but investigation of the adrenals in these exceptional cases appears to have been neglected.

That hirsutism in women is frequently associated with amenorrhea is the opinion of Lavastine[1] who submits a rather ingenious explanation. He states that hairs contain arsenic, iodine and phosphorus, and these abound also in the menstrual blood. When menstruation is scanty and these elements are retained in the body, the hypertrichosis might be regarded as a compensating reaction.

Hirsutism and diabetes is described by Achars and Thiers[2] in a woman who began to grow a beard at ten years of age and who was found to have diabetes at sixty-nine years. The patient had a heavy moustache, beard, and eyebrows, and necropsy, two years later, showed total sclerosis of the ovaries, hyperplasia of the suprarenals, chronic thyroiditis, and various changes in the pancreas. They conclude that the carbohydrate disturbance is a variable and inconstant element dependent upon polyglandular disturbance.

Weil and Plichet[3] report an instance of diabetes, fibroid ovaries and

[1] Paris Médical, 1921, **2**, 325.
[2] Bulletin de l'Académie de Médecine, 1921, **86**, 51.
[3] Bulletins de la Société Médicale des Hôpitaux, 1921, **45**, 312.

hirsutism in a woman, aged thirty-eight years, who died of galloping tuberculosis. The suprarenals in this case showed no lesion.

The **Suprarenals and Diabetes** is discussed by Tokumitsu,[1] who describes what he calls a new function of the suprarenal cortex, which becomes manifest when a ligature is thrown around the pancreatic duct. The cortex proliferates and hypertrophies, evidently as a compensating process. The medulla of the suprarenal, on the other hand, seems to have an antagonistic action to that of the pancreas. His research has confirmed that diabetes develops even with slight changes in the pancreas if the suprarenal cortex shows degenerative changes, while otherwise the diabetes develops only with pronounced changes in the pancreas.

The **Suprarenals in Epilepsy** is a relationship which is discussed in papers by Bruning,[2] Burke and Luttner,[3] Steinthal[4] and Gandor.[5] The subject is dealt with largely from the viewpoint of the treatment of epilepsy by extirpation of the suprarenals. Bruning, on the basis of Fischer's theory that the tendency to convulsions in animals is reduced by reduction in the suprarenal subtance, tried removing the left suprarenal in 9 cases. An improvement was effected in all cases, and in 2 of the patients there followed complete freedom from attacks. Gandor reports favorable results in 4 cases. Since, however, the longest interval is only three months, it remains to be seen how permanent these results will be. Steinthal reports complete failure in the 7 cases in which he tried this treatment and considers the removal of the gland of no value whatever in the treatment of epilepsy.

Addison's Disease. Absence of the right suprarenal gland has been recorded 6 times, according to Schnyder.[6] In 2, Addison's disease occurred when the other gland developed tuberculosis. Recently, Schnyder encountered a third case of aplasia of the right suprarenal. The patient was a man, aged sixty-eight years, with cancer of the larynx. The skin showed extensive bronzing and pigment spots in mouth. Necropsy showed congenital absence of the right suprarenal, but the single one found seemed to be normal.

Addison's disease in a child, aged four years, who showed at necropsy a ganglioneuroma of the left suprarenal gland, is reported by Figenschau and Berner.[7] The diagnosis during life had been tuberculosis of the abdomen. Although the abdomen was much distended, no ascites was found, the large tumor weighing 50 gm.

An autograph history of a case of Addison's disease by Muirhead[8] presents some interesting points. An abscessed kidney on the right side of long duration was removed in 1918. Recovery from operation was prompt, although complete restoration of health was delayed. During the subsequent eighteen months there were 6 attacks of arthritis

[1] Abstract, Journal of the American Medical Association, 1921, **77**, 823.
[2] Zentralblatt für Chirurgie, Leipzig, 1920, **47**, 1314.   [3] Ibid., 1920, **47**, 1410.
[4] Ibid., 1921, **48**, 878.   [5] Ibid, 1921, **48**, 881.
[6] Schweizerische medizinische Wochenschrift, Basel, 1921, **51**, 652.
[7] Norsk Magazin for Laegevidenskaben; abstract Journal of the American Medical Association, 1921, **76**, 1376.
[8] Journal of the American Medical Association, 1921, **76**, 652.

involving the right great toe, which was diagnosed as gout. Each attack was preceded or followed by rather severe gastro-intestinal disturbance. Following a rather severe attack bronzing of skin of hands and face developed and a diagnosis of Addison's disease was made. The blood-pressure was; systolic, 90; diastolic, 70. The urine examination revealed the presence of acetone. Neither adrenalin nor dried whole suprarenal gland nor pituitary gland had any beneficial effect. The symptoms continuing, the patient entered the Mayo Clinic. There the blood chemistry studied revealed, blood uric acid 6.9 mg. per hundred cc, and blood urea 44 mg. per hundred cc. His basal metabolic rate was about minus 30. He was placed on a purin-free diet, and in about two weeks the blood uric acid fell to 2.2 mg. per hundred cc. His digestive system did not tolerate milk or cream; but eggs, butter, sugar, and other foods of high caloric value were fairly well digested and he gained in weight on an average of one pound a week during the six weeks of his stay in the hospital. Adrenalin was administered hypodermically; the first injection of the contents of an ampule of a 1 : 10,000 solution produced a marked sensation of exhilaration and increased strength. The later injections of an equal amount produced less marked sensations. Injections of $\frac{1}{2}$ to 1 ampule, containing 1 cc of a 1 : 10,000 solution, were given twice daily during his stay in the hospital. Adrenalin solution by rectum was also tried. Improvement was observed almost from the beginning of hypodermic adrenalin medication. The earliest results were relief of the feeling of tension in the abdomen and an increased food tolerance. Soon an increase in strength and endurance was observed. A little later it was observed by the patient and others that the bronzing was disappearing. At the time of the report, Muirhead stated that he (the patient) was almost entirely clear of pigmentation, had but little gastro-intestinal irritability, had a fair endurance, and, still adhering to the purin-free diet and adrenalin therapy, was able to follow his occupation as a medical college teacher without difficulty. It is to be hoped that Muirhead will report further from time to time in regard to the progress of his case.

Keilty[1] reports a case of Addison's disease presenting the characteristic clinical symptoms of progressive weakness associated with bronzing of the skin. Pathologically, the case presented a typical localized and focalized tuberculosis of both suprarenals, with an arrested apical pulmonary tuberculosis of a probable unassociated nature. The direct smear from the suprarenal showed the presence of tubercle bacilli in large numbers. Animal inoculation with crushed material from the suprarenal produced experimental tuberculosis from which tubercle bacilli were obtained in culture.

As Keilty points out, the study of the case presented several interesting features. In the first place, the presence of an advanced and directly confined tuberculosis in both suprarenals, and the finding of a completely arrested and healed tuberculosis in the apices of the lungs is a hard one to explain. There has evidently been no fresh activity

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[1] American Journal of the Medical Sciences, 1922, **163**, 282.

arising from the lungs. The apical infection may have preceded the suprarenal infection, or may have been coincident with it, or even the so-called healed lesions may have given up virulent tubercle bacilli which have secondarily lodged in the suprarenals. That this disease, at one time, must have been a bacteriemia, at least of a temporary nature, is quite evident. It would seem that the pulmonary lesions occurred at one time and were completely arrested, while the suprarenal lesion received its dosage through another portal of entry not apparent at the time of autopsy. The question as to whether a strain of tubercle bacilli with a predilection for the suprarenal is only a supposition, and, on the other hand, any chemical combination which the suprarenals might have had in attracting the tubercle bacilli to that particular site would, it seems, be a decided possibility. The complete absence of tuberculosis elsewhere in the body, in the presence of such an active lesion as found in the suprarenals, offers a further field for study. That the organisms had any predilection for the suprarenal gland is more certainly ruled out by the fact that when inoculated into the guinea-pig they produced in duplicate the usual experimental tuberculosis.

THE SPLEEN.

Splenic Functions. The spleen and digestion was studied by Inlow,[1] who states that from the earliest times the spleen and the stomach have been supposed to possess some close interrelationship. The ancients attributed to the spleen, among other functions, that of warming the stomach, an opinion which as late as 1723 was reaffirmed by Stukeley in these words: " Does not nature proclaim its (spleen's) great eminence by its situation, being placed on the left side of the stomach, where digestion is chiefly performed, and closing it up, as it were, like the door of a furnace, that it may have an equable warmth quite around so that the spleen alone in this single requisite of heat is opposed to all the rest of the bowels put together that encompass the stomach?" He further adduced as proof of this assumption the "notorious" and "terrible" effects produced by eating ice and snow liquors in hot countries! Is this not in accord with the fancy entertained by the ancients "that creatures which drink much have larger spleens, whose business it is to warm the stomach against such a quantity of cold fluid?"

Baccelli, in 1868, demonstrated a gastrosplenic circulation through the vasa brevia, and first put forward the theory that the spleen plays a role in the elaboration of pepsin. Subsequent studies have been contradictory. Inlow's studies concerned the gastric secretion findings before, and after, splenectomy on 3 dogs with accessory stomach pouches (secretory meal of meat) and on 2 similar dogs serving as controls. Removal of the spleen in these experiments caused no noteworthy changes in gastric secretion except a slight diminution in the quantity of gastric juice obtained. Inlow concludes, from his experi-

[1] American Journal of the Medical Sciences, 1921, **162**, 325.

mental inquiries and a critical review of the literature, that a definite pepsinogenic function of the spleen has not been demonstrated and that the relation of the spleen to gastric secretion is probably merely vascular, the diminution in the amount of juice secreted after splenectomy being attributable to decreased gastric blood supply from injury to the gastrosplenic circulation.

The ERYTHROCYTE-DESTROYING FUNCTION OF THE SPLEEN was studied by Frey,[1] who found, in experiments on dogs, that the blood from the splenic vein contains fewer erythrocytes than the arterial blood or the blood from a vein in the ear. The difference in the number of erythrocytes between the arterial and the splenic vein blood becomes larger when the resistance of the red corpuscles has been reduced by a blood-poison, such as ether. The difference grows less and less when the resistance of the red corpuscles is enhanced by substances such as phenylhydrazin. The hemoglobin percentage was alike in both splenic vein and ear vein blood in dogs. As there are fewer erythrocytes in the splenic vein, this finding in regard to the hemoglobin seems to suggest that free hemoglobin is present in the serum of the splenic vein blood.

ENLARGEMENT OF THE SPLEEN OCCURS IN EXPERIMENTAL ACIDOSIS, according to the studies of Householder.[2] This same acidosis produces an associated anemia by favoring hemolysis. An increased hydrogen-ion concentration favors the hemolytic action of hemolytic agents. The experimental results suggest that the enlarged spleen may be due either to an increase in its function as a hemoglobin-destroying organ as a result of the hemolysis, or, as a result of its hyperfunction, as a hematopoietic organ in combating the anemia accompanying an acidosis. Of clinical value is the possible influence of these studies in the interpretation of such conditions as uremia and heat stroke, etc., in which splenic enlargement, anemia, and acidosis have been reported as present in varying degree.

ENLARGEMENT OF A SPLENCULUS TO SIZE OF A NORMAL SPLEEN. This interesting finding is reported by Eccles and Freer.[3] A football player, aged twenty-one years, sustained an abdominal injury requiring operation, at which time a ruptured spleen was found and removed. The spleen was larger than normal, weighing 13 ounces, a condition attributed to malarial fever contracted previous to the accident. After a tedious convalescence, he was able to return to work and continued in good health for eight years, after which he began to have some attacks of weariness, and was found to have an evening temperature. It was considered by his medical advisers that this might be due to some obscure form of tuberculosis. His blood-count was virtually normal. In general health he appeared well, and there was no anemia or temperature elevation. There was a wide gap in the upper third of the left rectus, and, on coughing, a marked proturberance of abdominal contents took place. Upon opening the abdomen, some adhesions of the

[1] Deutsches Archiv für klinische Medizin, Leipzig, 1920, **133**, 223.
[2] Journal of the American Medical Association, 1921, **76**, 1556.
[3] British Medical Journal, 1921, **2**, 515.

omentum were found and separated. Then, to the astonishment of all present, a well-formed, normal-looking spleen was seen in the usual position. The shape, size, notch, color, and consistency all appeared to be that of a normal spleen. That a splenculus may enlarge, after the removal of an ordinary spleen, is well known, but the rarity with which such an enlarged organ is actually seen, leads the authors to place this case on record.

Splenic Anemia. BANTI'S DISEASE. The clinical features of splenic anemia which have been reiterated by Moynihan[1] are: (1) a very chronic course; (2) a slowly progressive enlargement of the spleen; (3) changes in the blood (of the type found in secondary anemia); (4) the tendency to hemorrhages; (5) affection of the liver; (6) an unknown causation and (7) other phenomena chiefly of negative importance. Banti considered the disease as possessing clinically three stages, merging gradually into each other. These stages are, first, the stage in which there is gradual enlargement of the spleen and a secondary anemia, the duration being three to twelve years; second, the stage in which the liver gradually enlarges and the amount of urine undergoes progressive diminution—the duration is brief; and thirdly, the stage in which the liver gradually shrinks in size and ascites appears, the symptoms being those of an ordinary atrophic cirrhosis. The duration of this final stage is between one and two years. The disease is invariably fatal, and death occurs either from hemorrhage or from autointoxication from hepatic cirrhosis.

Canelli[2] reports an instance of Banti's disease in an infant of fourteen months. By contrast, as far as age is concerned, is the report by Garin[3] of a man, aged sixty-seven years, who had been under observation for eleven years and who died of acute miliary tuberculosis. According to Garin, the testimony seems to favor some primary infection localizing in the spleen, permanently injuring its structure and function after the infectious process has died out. The toxins generated by the abnormal metabolism in the spleen are responsible for the further injury of the spleen and of organs directly connected with its circulation, the liver in particular. In his patient the cirrhosis of the liver occurred early in the course, although ascites did not develop until nine years later. There was no hemorrhage at any time, and even at the tenth year there were 3,500,000 erythrocytes and 40 per cent hemoglobin.

Moynihan,[4] in his Bradshaw Lecture, discusses the pathogenesis of Banti's disease in a fashion which clarifies present knowledge. To quote him at length: The fact of utmost significance in connection with the causation of this disease is that it is cured or arrested by early removal of the spleen. This fact may be accounted for either by assuming that the disease is primarily and essentially located in the spleen, or by assigning to the organ the role of modifying the action of some agent situated elsewhere in the body. If the disease is primarily splenic, a

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[1] Lancet, 1921, **200**, 157.   [2] Pediatria, Naples, 1921, **29**, 897.
[3] Revista Critica de Clinica Medica, 1921, **22**, 1.
[4] Lancet, 1921, **200**, 157; also The Spleen and Some of its Diseases, 1921, W. B. Saunders Co., Philadelphia.

search for a specific microbic infecting agent should ultimately be successful. Hitherto, no convincing evidence of this has been found, although Hollins has argued strongly in favor of incriminating the colon bacillus. There is scope for further research in this direction, and the organ removed during life, if straightway examined, should provide profitable material for routine bacteriological investigation. The enlargement of the spleen has been attributed to excessive hemolytic activity by those who consider the disease to begin in some other part of the body. But such a view does not sufficiently explain the fibrosis which is the outstanding histological feature of the disease. A chronic infective process would account for the enlargement as well as the fibrosis, and accord better with the absence of undue hemolysis of the red blood cells. In splenic anemia, the red cells never show "fragility." If there is a change, the corpuscles may show increased, rather than diminished, resistance. The anemia, in like manner, may be regarded as an incident or as an essential part of the disease.

Rolleston, a very distinguished authority, does not regard the anemia as primary; he believes it to be secondary to attacks of very severe hemorrhage, chiefly because he finds that regeneration of blood takes place after these events. This view, however, is, I think, subject to the criticism that such severe hemorrhage is not invariable, and that the substance elaborated in the spleen need not be capable of affecting the bone marrow until after it has left the liver, where it has undergone modification. Further, whatever the poisonous substance may be, it need not completely arrest blood-cell development. A parallel case, according to Moynihan, is furnished by subjects of leukemia in which an intercurrent infection intervenes, with a temporary restoration of the normal blood picture.

Hollins regards the disease as being due to an active "intoxication" produced by the colon bacillus, whose toxin brings about the anemia, while its actual presence in both spleen and liver accounts for the fibrosis. This view would put every kind of cirrhosis of the liver on the same level, because "colilysins" could not be expected to vary radically in their action. The facts would be better met were it suggested that the spleen harbors various organisms, some of which only excite a local fibrosis, others induce a simple cirrhosis of the liver, and still others produce that form of cirrhosis associated with Banti's disease, with a toxic anemia and other specific symptoms.

In respect to the hemorrhage, which is so conspicuous and alarming a feature of some cases, Rolleston considers that the enormously distended vasa brevia rupture into the stomach as a result of the torsion of the splenic vein caused by the great bulk of the organ. This opinion, according to Moynihan, is certainly correct in many cases. The hemorrhage is so profuse and so swiftly escapes from the stomach that large vessels must be implicated. Such vessels as Rolleston describes are often seen in operations upon cases of splenic anemia when abundant hematemesis has occurred. But this cannot, as Moynihan states, be the whole explanation. The relationship between the enlargement of the spleen and gastric hemorrhage is cryptic, since removal of the spleen

may cure a patient whose life has been jeopardized by severe and recurrent hemorrhages from the stomach. However, gastric hemorrhage is known also to be toxic in origin in certain cases, as, for example, those in which there is a lesion in the appendix, intestine, or gall-bladder; and those also in which the lesion lies in the spleen or liver, or both. A toxic factor must therefore be considered.

The discovery of the cause of the splenic condition removes the case from the category of splenic anemia. Thus, Bufalini[1] reports the case of a woman, aged thirty-seven years, whose spleen was removed on the assumption of Banti's disease. Subsequent study of the spleen revealed a tuberculous lesion. Bufalini states that there are five similar cases on record.

In the diagnosis of splenic anemia, Moynihan states that the most common mistake is the making of a diagnosis of gastric or duodenal ulcer. Five patients suffering from splenic anemia have been referred to him with the diagnosis of these diseases. The absence of a clear history of dyspepsia, the presence of an easily palpable spleen and the blood changes quickly revealed the true condition. The contrary mistake may likewise be made. In any doubtful case the roentgen-ray examination would almost certainly clear away the uncertainty and demonstrate the presence of a chronic gastric ulcer.

The close relationship of spleen and liver in Banti's disease is not unique for that condition. The spleen and liver are interrelated closely normally and in many abnormal states. Moynihan[2] has stressed this relationship in his recent monograph.

Mayo[3] refers to *the spleen in portal and biliary cirrhosis.* He states that in portal cirrhosis the spleen may play a prominent part in the etiology, and splenectomy in properly selected cases may be of great benefit. By splenectomy not only the supply of toxic material, if there be such, is cut off from the general circulation but also the portal blood stream is reduced by substraction of the amount of blood poured into the portal vein from the spleen, about 25 per cent of the total under normal conditions. After the removal of some of these huge spleens, an enormous reduction of the portal circulation takes place, so that the hepatic cells may be relieved of a sufficient overload to enable them to function normally and, moreover, the liver under favorable circumstances has power regeneration. Eleven patients with portal cirrhosis were subjected to splenectomy, with 4 deaths in the hospital. All of these patients were in the last stages, with ascites, hemorrhage from the stomach, and so forth. Only in such grave cases was the operation considered justifiable. After the removal of the spleen, the omentum was spread in the denuded splenic area and fastened in the abdominal wound in order to give the additional benefits of the omentopexy of Talma-Morison and Drummond which the writers have occasionally found of great benefit in relieving the ascites and other evidences of portal obstruction. Four of these patients were markedly benefited.

[1] Reforma Medica, Naples, 1921, 37, 434.
[2] Ibid.
[3] Journal of the American Medical Association, 1921, **77**, 34.

One patient is now alive after five years. In early operations, the operative mortality would be small and the end-results much better.

In biliary cirrhosis—from ascending infection from gall-bladder and ducts, pancreatitis, or focal infections elsewhere; or in association with portal cirrhosis; or secondary to splenic lesions—the relation of the spleen may be important. As Mayo points out, it is difficult, in some cases of biliary cirrhosis, to exclude latent hemolytic icterus as a contributing factor. In 20 of 32 cases of hemolytic icterus in which were performed splenectomy, gall-stones were present, usually bile-pigment stones, the result of the enormous amount of pigments derived from the unnecessary red blood cell destruction in the spleen. Splenectomy was performed in 6 cases of primary biliary cirrhosis with greatly enlarged spleens. In these cases the cause of the biliary infection, so far as could be learned, had been removed previously—such as gall-stones and focal infections—without marked relief. All of the 5 patients who recovered were greatly benefited; 3 are alive two years; 2, three years and 1, five years after splenectomy.

Splenectomy for splenic anemia is unquestionably an operation of value. Mayo states that among 249 spleens removed in the Mayo Clinic for all causes, there was a mortality of 10 plus per cent. Of the 249 splenectomies, 71 were for splenic anemia of unknown origin, with 9 deaths. In addition, splenectomy was performed in 38 cases for splenic anemias of known origin, as follows:

Chronic Sepsis. Eleven spleens which had become greatly enlarged in the course of chronic general sepsis following septic arthritis, tonsillitis, phlebitis and osteomyelitis, with 3 deaths in the hospital. The other patients were cured or greatly benefited.

Syphilis. Splenomegalia is often found with chronic syphilis. Some observers who have had wide experience with syphilis have believed that the large majority of cases of so-called splenic anemia are syphilitic in origin. At the Mayo Clinic, removal of spleens was practised in 6 of this kind, with 1 death. Patients who had resisted thorough syphilitic treatment and in whom chronic anemia was a manifest sign, were at once made amenable to treatment and quickly recovered.

Splenic Anemia in Children and von Jaksch's Disease. Eight spleens in such children were removed without an operative death, and, when the condition was not advanced, cure has followed.

Chronic Malaria results in a splenomegalia with generalized fibrosis and thrombophlebitis that we recognize as a form of splenic anemia. The removal of the enlarged spleen renders the malarial treatment more effective. It is understood, of course, that the removal of the spleen does not cure the malaria, but removes a very serious complication, which is one of the means by which the death of the patient is brought about.

There can be no doubt that at the present time, in properly selected cases, with early operation, a low mortality and satisfactory end-results can be expected, not only in the splenic anemia of unknown origin, but in those of known origin as grouped above.

Chronic Splenitis. In the Schorstein lecture by Gibson[1] is to be found an excellent review of the conditions grouped as chronic inflammatory lesions of the spleen. The lecture is limited to those conditions in which directly, or indirectly, the etiologic factor is infection. The spleen becomes infected in three ways: (1) As the result of a general blood infection which subsequently may become restricted to the spleen, as in syphilis and tuberculosis; (2) because the spleen in destroying blood cells comes into fuller contact with the organism, as in malaria and kala-azar; (3) being the largest lymphatic gland in the abdomen, it may be the point of attack in any gastro-intestinal infection. Gibson discusses in detail the local and general effects of splenic lesions.

We shall refer to but two types which he discusses: *primary syphilitic splenomegaly* and *primary tuberculous splenomegaly*. Gibson collected 25 cases of the former and sums up these characteristics. The anemia tends to be of the chlorotic type, as in the typical splenic anemia, and the red cell count drops to just over 1,000,000. French's patient approached the clinical picture of pernicious anemia, though actively chlorotic in type. Schulmann and Weissmann's patient had polycythemia. The white cell count varies. One of Osler's patients had the blood picture of leukemia; in the other cases, white cells vary from 4560 per c.mm. in Stevenson's case to 21,000 in French's. The leukocytosis recalls that after splenectomy for trauma we must keep in mind the possibility that a spleen may be so damaged by disease that the same effect at compensation is demanded from other white cells in the body which we see after splenectomy. Further, such compensation having been established before operation, we should not expect such a marked leukocytosis afterward.

As regards jaundice, both of Giffens's patients had suffered from transient attacks. Similar attacks of jaundice are reported in Pollitzer's and Osler's patients. Four cases (Giffen, Coupland, Hartwell and Osler) are reported with hematemesis and in 2 epistaxis is mentioned. Four patients are reported as having had ascites (Osler, Coupland, Queyrat, and Groves).

The reaction to antisyphilitic remedies, including arsphenamine, is startling in its unevenness. In the patients of Schulmann and Weissmann, Perussia, Pollitzer and Clark, the results were extremely satisfactory, while in others (Giffen, Hartwell, French) it produced no amelioration. Other cases described, with enlarged spleen, positive Wassermann and chlorotic anemia, have been uninfluenced by arsphenamine and other remedies, and we must search for some factor which enables us to explain why one can be cured and the other not. We know that some enlarged syphilitic testicles can be cured only by excision and the cerebral gumma is not always amenable to specific treatment.

Tuberculosis of the spleen (tuberculous splenomegaly), according to Gibson,[2] in its primary form is very uncommon. He refers to the report by Winternitz, in 1912, which contains a complete record of the 51 cases reported to that time. Some of these are not sufficiently proved to be

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[1] Lancet, 1921, **2**, 885.   [2] Ibid.

included in Gibson's survey. There are, however, 21 clear cases in which tubercle bacilli have been found in the primary tuberculous splenomegaly.

Gibson summarizes the clinical characteristics as follows: The *symptoms* are general and local. In about 25 per cent of cases there is fever, sometimes as a marked feature. Sweating and collapse are mentioned and very constantly loss of weight, weakness, and great lassitude. Locally, there is pain and a sensation of tumor and weight in the left side. The pain may vary in its incidence with positions and movements of the body, or may come on only during digestion. The proximity to the diaphragm may cause pain on respiration. The majority of cases are very chronic, but short illnesses terminated by death have been recorded. There are 15 patients recorded in the literature that have been subject to operation, with 9 cures. The disease is rarely strictly primary in the spleen, since other organs show some signs of tuberculosis. Thus, of Winternitz's cases, nearly half showed pulmonary changes, and 5 had enlargement of other glands. Other clinical features noted in the literature have been an enlarged liver, with cirrhosis, ascites, caries of the spine, meningitis, and intestinal ulceration. Blood changes are either absent altogether or very moderate. In 9 cases in which the condition of the blood is mentioned, 6 were normal and 5 had a moderate degree of anemia of the chlorotic type. The lowest red count is 3,200,000, and the lowest white count is 2500, the average white count being 5000. The lowest hemoglobin figure is 50 per cent. The blood changes are not a striking feature of the disease.

It is a current opinion, according to Gibson, following Winternitz's critical review, that polycythemia is one of the characteristics of a tuberculous splenomegaly. But in eliminating from the list of cases those whose tuberculous origin is not adequately proved, no case shows an abnormally high blood count. Of the doubtful cases, that of Moutard-Martin and Lefas, whose blood showed 8,200,000 red blood cells and 31,428 white blood cells, there was naked-eye evidence of tuberculosis in many other organs than the spleen, and even admitting the tuberculous origin the relation between tuberculosis of the spleen and the polycythemia is not clear. In Carminotti's case there was a much scarred spleen, but no other evidence of tuberculosis, and caries of the spine. The counts were: red blood cells, 7,000,000; white blood cells, 6000. The other 4 cases recorded by Winternitz have red cell count of 6,000,000. On these grounds, we cannot yet admit that polycythemia is proven as an association with a tuberculous splenomegaly. On general grounds, a polycythemia may be expected if there be obstruction in the portal vein; such, however, cannot be used in any case as an argument for a tuberculous origin of a chronic splenitis. When tuberculosis affects the thorax as well as the spleen, there are other possibilities for a mild polycythemia. Implication of the liver is not uncommon. Of Winternitz's 17 positive cases, tubercles were present in 10, and there was atrophic cirrhosis in 1.

Sotti describes the liver changes in these cases as frequent. The common anatomical changes are fatty degeneration, necrosis, swelling

and thickening of the collagen substance, and sometimes small lymphatic accumulations, and he looks upon interstitial hepatitis as dependent upon changes in the splenic vein. Jaundice as a symptom of tuberculous hepatitis in these cases is rare and I have found only one mention of it, in Winternitz's own case. Hematemesis is not recorded in any case, unless we admit that of Paulicek, in which tubercle bacilli were not found. This case had a hematemesis at six years, when the illness commenced. Glands are mentioned as enlarged in 4 cases, and the lungs were affected in 6 cases.

Traumatic Lesions of the Spleen. *Spontaneous rupture of the spleen* is less common than that which occurs as a result of definite injury. Connors[1] reports an instance of spontaneous rupture. Following splenectomy, the patient made a good recovery. Three months later he returned complaining of attacks of indigestion, with eructations of gas. At the time of these attacks, he had considerable pain in the abdomen in the region of the umbilicus. For some time, he was unable to stand in the erect posture on account of a dragging sensation in the region of the mass in the abdomen. The pain was markedly increased at every attempt to change his position. He had a sensation of something swelling inside him, which increased the pain, and when able to belch gas was considerably relieved. At operation, a large, cystic mass was found which seemed to spring from the location of the spleen, and was bulging between the stomach and the splenic flexure. Connors believes this was a pancreatic cyst which was the result of the injury to the pancreas at the time of the splenectomy.

Massari[2] warns as to the vulnerability of the malarial spleen, and the possibility of rupture due to a slight trauma. In addition to his own case, he collected 20 other cases of operation for rupture of the spleen in malaria, 14 of which recovered and 6 died. The prognosis depends on the rapidity with which the operation is performed after the accident has occurred. Leighton[3] reports a case of spontaneous rupture of a malarial spleen and gives an abstract of the reported cases from 1842 to 1921.

Torsion of a Wandering Spleen in a child, aged six years, is reported by Southam.[4] The lad was admitted to the hospital with a diagnosis of acute appendicitis. Under the anesthetic, a large and freely movable tumor was palpable in the right iliac fossa. The tumor was found to be an enlarged and congested spleen. The organ was without difficulty removed. Convalescence was uneventful. The spleen was found to weigh fourteen ounces, three to four times the usual weight of the organ at this age. The child showed no evidence of rickets or congenital syphilis, and the other abdominal organs appeared at the operation to be normal in size and position. The ectopic spleen is said to be usually found on the left side of the abdominal cavity; in this case it was well to the right of the median line.

[1] Annals of Surgery, 1921, **73**, 1.
[2] Wiener klinische Wochenschrift, October 14, 1920.
[3] Annals of Surgery, 1921, **73**, 13.
[4] Lancet, May 26, 1921, 642.

Hematopoietic Splenomegaly with Marrow Sclerosis is the name which Wade[1] gives to the condition found in a patient who came under his observation. Epigastric discomfort led to the abdominal examination and finding of the enlarged spleen. Evidences of a pulmonary tuberculosis were present, associated with loss of weight and remittent diarrhea. He was able to be about and had no fever. The Wassermann test was negative and no malarial parasites found. The blood examinations revealed little of interest except 8 per cent large mononuclears. The spleen was removed. The patient died on the fourth day after operation. Examination of the spleen revealed very active hemopoiesis, with here and there discrete nodules of marrow-like tissue wholly foreign to splenic structure. There was complete lack of hemopoietic activity on the part of the bone marrow, much of which had undergone marked osteofibrosis. Some hemopoietic activity was found in the liver and the prevertebral lymph nodes.

Telangiectatic Splenomegaly. According to Symmers[2] there is a systemic disease characterized by extensive proliferation of the endothelium of capillaries, particularly involving organs that belong to the hematopoietic group—the spleen, bone marrow, liver and the lymph nodes. The most striking feature of the disease is the massive enlargement of the spleen due to endothelial hyperplasia, with the production of new capillaries and the subsequent formation of telangiectases, identical or related histologic changes being apparent in the other organs named and, occasionally, in organs beyond those of the hematopoietic system. In the spleen and lymph nodes, the proliferative changes in the capillary endothelium appear to rise in vessels that are native to the part. In other instances the same sort of cells may be seen infiltrating and distending capillaries, notably in the skin, bone marrow and liver; but whether these cells are produced *in situ* is not apparent. The disease is neither frankly neoplasmic nor strictly inflammatory, but presents features incident to both and, perhaps, is best included in that group which occupies a position intermediate between neoplasia and inflammation, taking its place, in this regard, with Hodgkin's disease, mycosis fungoides, Cohnheim's pseudoleukemia, Sternberg's leukosarcoma, Gaucher's splenomegaly, and the like.

The case reported by Symmers was that of a man, aged seventy-five years, a carpenter, who died seven days after admission to the hospital. He had been complaining of a persistent, dull aching pain under the left costal margin for a period of about three and a half months. Physical examination revealed beneath the ribs on the left side, corresponding to the position of the spleen, a mass, the edge of which was rounded and reached to the level of the umbilicus and as far forward as the midsternal line. The mass moved with respiration and was extremely tender to the touch and perfectly smooth. Beneath the skin covering the right pectoral muscle, just below the shoulder, were two pea-size nodules which were freely movable. In the right upper quadrant of the abdomen two larger, but otherwise similar, masses were to be felt. None of these

[1] Journal of the Philippine Islands Medical Association, 1921, **1**, 143.
[2] Ibid., **77**, 2019.

were tender. The skin covering them was greenish-yellow but, after palpation, became hemorrhagic within a few hours. On the day before death, the skin of the anterior abdominal and thoracic walls suddenly exhibited an extensive network of minute bluish or bluish-red, intercommunicating streaks which corresponded, apparently, to congested and dilated capillaries. The white blood cells numbered 5400. The differential count was: polymorphonuclear leukocytes, 69 per cent; lymphocytes, 20 per cent; eosinophils, 1 per cent; hemoglobin, 80 per cent.

The Hemal Nodes. The preponderance of evidence, according to Symmers[1] seems to favor the view that the hemal nodes are more closely related to the spleen, structurally and otherwise, than to the lymph nodes proper—that they represent a succession of dimunitive spleens corresponding to the auxiliary lymphomatous deposits that normally exist in the interstitial tissues of many organs. Symmers states that tumors in human beings springing from the hemal nodes have not hitherto been described. He reports the studies of 2 such cases and concludes that there is a form of malignant tumor belonging to the lymphocytic group in which the naked eye and histological characteristics are such as to indicate derivation from the so-called hemal nodes, that is to say, the tumor arises in that locality where the hemal nodes are most frequently encountered, has a distinctive reddish or bluish-red color and, microscopically, more or less faithfully counterfeits the histology of the hemal nodes in that it is composed of groups of lymphoid cells separated by innumerable distended blood sinuses with, or without, a supporting reticulum of connective tissue.

Two forms of neoplasmic growth are described in this paper—one occurring as a solitary mass without metastases, but attended by secondary nodules arising regionally, and hence to be classified as locally malignant; the other giving rise to multiple selective subperiosteal metastases, and hence highly malignant.

THE BLOOD.

Hemato-respiratory Functions. In 1918, Haggard and Henderson[2] commenced work which has been reported at various times since then in the *Journal of Biologic Chemistry* under the general title of "Hematorespiratory Functions." Papers comprising Studies VII to XI appeared in December, 1920. These studies are of twofold interest to the readers of this section of PROGRESSIVE MEDICINE: First, in relation to the hydrogen-ion concentration of the blood which we have discussed in previous pages; and, secondly, as they concern the specific functions of the hemoglobin and red cells. Haggard and Henderson state that, "Hemoglobin plays almost as large a part in the transportation of CO_2 as it does in that of oxygen. It does not itself combine directly with CO_2 to any great extent, however, but under pressure of CO_2 it absorbs HCl, and thus provides alkali, which in the plasma is chiefly Na from

[1] Archives of Internal Medicine, 1921, **28**, 467.
[2] Journal of Biologic Chemistry, 1920–21, **45**, 189, 199, 209, 215, 219.

NaCl, to form bicarbonate. As CO_2 is given off in the lungs, NaCl is reformed from $NaHCO_3$."

"From any blood, therefore, plasmas of widely varying content of alkali are obtained, depending upon the tension of CO_2 at the time of centrifuging. Each of these plasmas has various alkali values with varied tensions of CO_2. The relation of the primary and secondary dissociation curves of the plasma to each other and to the curve of the whole blood are here exemplified.

"A quality of normal blood from a resting animal is that variations of CO_2 tension (in the presence of ample oxygen) call nearly the same increase of alkali into use in unit volume of the blood as in unit volume of its unseparated plasma. Thus, the bicarbonate content of the corpuscles (apart from the effect of variations of oxygen) rises and falls with that of the plasma around them. But this does not hold at abnormally high tensions; and at very low tensions, as will be shown in later papers, the blood undergoes an irreversible alteration. The parallelism of alkali variations in corpuscles and plasma affords, therefore, a convenient test as to whether or not a given blood sample is normal.

"It is probably by means of the quality of gain and loss of bicarbonate that the P_H inside the corpuscles and that outside them in the plasma are kept the same, or at least in uniform relation. The P_H indicated by the primary plasma curve at various tensions of CO_2 in the blood is particularly significant.

"It thus appears that the corpuscles dominate the plasma so powerfully that the alkali of the (unseparated) plasma at a certain tension of CO_2 is essentially an expression of the alkali-producing power of the corpuscles. The plasma alkali is only a part of the total alkaline reserve of the blood. The chief buffer is the hemoglobin. The extent to which the corpuscles are loaded with HCl is indicated by the amount of alkali which they call into use out of NaCl at a certain tension of CO_2. That is the CO_2 capacity of the blood."

In another study, Haggard and Henderson conclude that "Centrifuged corpuscles suspended in saline solution and exposed to a tension of CO_2 produce in the saline solution an amount of alkali only a little (one-fifth or one-tenth) less than that called into play in the plasma before centrifugation at this CO_2 tension.

"Corpuscles may have their load of HCl increased or decreased by suitable equilibrations. The alkali producing power of the corpuscles is adjusted accordingly. When suspended in a saline solution, corpuscles already heavily loaded with HCl call forth less alkali at a given tension of CO_2 than less loaded corpuscles.

"The total capacity of the corpuscles for acid is equivalent to an amount of alkali several times greater than that in the plasma of normal blood. This capacity is controlled immediately by the tension of CO_2 and concentration of H_2CO_3 and presumably the P_H in the blood. When the H_2CO_3 is increased there is an almost proportionate increase of $NaHCO_3$ and the change in the CO_2 ratio ($H_2CO_3:NaHCO_3$) and P_H is correspondingly slight.

"When whole blood is equilibrated at a very high tension of CO_2 the alkali-producing power is not (as might be supposed) exhausted. The alkali called into use at such tensions is therefore not a measure of the total potential alkali-producing capacity of the corpuscles. It is merely a measure or approximation of what they can do in the existing plasma (high in $NaHCO_3$), against which they are balanced."

In their third paper, Haggard and Henderson show that when in animals overventilation of the lungs is carried so far that the arterial CO_2 tension is reduced below the critical level, an irreversible reduction in the CO_2 combining power of the blood occurred. Thereafter, restoration of CO_2 to the blood even by inhalation of CO_2 in air was ineffective, and death always followed.

They conclude that when the blood is exposed to a tension of CO_2 below a critical level it undergoes an irreversible, or at least not readily reversible, change. Thereafter, if it is equilibrated with a normal tension of CO_2 it combines with distinctly less CO_2, and presumably produces correspondingly less $NaHCO_3$, than it did at this tension previously. Defibrinated blood is even more prone to such changes than oxalated blood, but oxalated blood likewise shows them.

Hemophilia. A case of pronounced hemophilia treated by injections of *horse-serum* whose cure has lasted for twelve years, is reported by Weil.[1] The treatment was begun in 1909, when the patient was seven years old. Fifteen injections of horse-serum were given at intervals of two months for each injection. The blood coagulation time, when treatment was started, was three and one-quarter hours. At that time he had frequent joint pains and probably hemarthroses. At present, the coagulation time is five minutes. The patient was a member of a family of bleeders of Tenna, first described in 1841 by Matzenbrecher. From the 8 cases of hemophilia which Weil has successfully treated, it is concluded that the disease is not a malformation of the blood, but a curable malady, and that possibly even its hereditary transmission may be prevented. Stewart[2] states that serum therapy of hemophilia gives the best and most permanent results. The serum should be reasonably fresh, that is, less than two weeks old. Human serum or that from the horse is advised, and the intravenous method of administration is considered best. Ten or 20 cc are injected, and repeated in four weeks. The local application of serum by plugging by compress aids in the arrest of hemorrhage. Transfusion is chiefly for posthemorrhagic anemias.

Polycythemia. An exhaustive monograph on *Polycythemia, Erythrocytosis and Erythremia (Vaquez-Osler's Disease)* by Parkes-Weber has appeared during the past year. This monograph contains a critical review of the literature upon the subject to the present time. The term *polycythemia rubra*, or, for short, polycythemia, signifies an increase in the number of the red blood corpuscles, and is divided into two forms, which correspond respectively to leukocytosis and leukemia in the case of the white blood corpuscles, namely: (1) erythrocytosis,

[1] Bulletin et Mémoires Société des Hôpitaux de Paris, 1921, **37**, 1018.
[2] Journal of the Michigan State Medical Society, 1921, **20**, 317.

in which the increase of cells is secondary to some definite factor, such as concentration of the blood by diarrhea, vomiting or sweating; or compensatory, as in the polycythemia of high altitudes, and in cardiac or pulmonary disease with cyanosis; and (2) erythremia in which a well-marked, persistent, relative and absolute increase in the number of red blood corpuscles is due to a primary disorder of the erythroblastic tissue in the red marrow of bone, and so analogous to the leukoblastic activity in leukemia. This is the condition originally described, in 1892, by Vaques, of Paris, and brought more prominently to our notice by Osler, in 1903 and 1904. Although the spleen is nearly always enlarged, Weber considers that the synonym, splenomegalic polycythemia, should only be used in a clinical sense, that is to say, as signifying a symptom-group composed of polycythemia not obviously secondary to blood stasis, and of splenomegaly for which no local cause, such as thrombosis of the portal or splenic vein, is suspected—for necropsy may show that the splenic enlargement is due to some definite lesion, such as syphilis or tuberculosis, and the associated polycythemia may be due to blood stasis and so not true erythremia. The cases described by Geisbock as polycythemia hypertonica appear to Weber to be examples of secondary polycythemia in some way or other intimately connected with high arterial blood pressure. Though he insists at length on the forms of secondary polycythemia, Weber takes issue with Warthin's contentions that erythremia is always secondary, and that Ayerza's disease, or cyanosis with secondary polycythemia due to arteriosclerosis of the pulmonary artery, is usually due to syphilis.

Gitlow[1] reports a case of polycythemia vera in which the blood examination revealed 140 per cent hemoglobin, 6,740,000 red cells and 14,000 white cells, of which 83 per cent were polynuclears. The symptoms which the patient presented were dizziness, easy fatigue, neuralgic pains over various parts of the body and constipation. Occasionally, colicky pains occurred in the epigastrium associated with the vomiting of bloody mucus. The gums bled easily and at times epistaxis occurred. The menstruations were normal up to the time of the menopause at forty-four years. The patient appeared ruddy. Gitlow could establish no etiological factor.

TREATMENT OF POLYCYTHEMIA by the roentgen ray is discussed by Pendergrass.[2] The technic which he advises is as follows: (1) The applications are made primarily over the bones of the entire skeleton, except the bones of the head, these being omitted, due to the likelihood of the loss of the hair in this region. (2) Each area is exposed regularly and systematically, and it is recommended that the maximum dose be distributed over three successive days rather than at one time. (3) Exactness in dosage is essential because we do not wish to destroy the bone marrow but to inhibit the formation of the red cells, just as in hyperthyroidism we do not wish to destroy the secreting cells of the thyroid but to inhibit their hyperactivity. (4) Frequency: Daily exposures are advocated until the series is completed. Two areas may

[1] Medical Record, 1921, **99**, 227.
[2] American Journal of the Medical Sciences, 1921, **161**, 723.

be exposed at one time, as in polycythemia we do not get the toxemia we get in leukemia. (5) Direct exposure of the entire spleen is given after the bones of the skeleton have been completed twice, and at this time we only give a stimulative dose. (6) Duration of the treatment depends upon the individual patient. However, three series are usually required before any stability in the blood counts is noticed. After the patient has received three series he should come in at intervals for inspection, and blood counts should be taken so that any premonitory signs, such as increasing red cell counts, can be discovered early. Pendergrass admits that further study is necessary to ascertain whether there is an increase in hemolysis or a decrease in the formation of the red cells, or both, during roentgen-ray therapy of the bone marrow. He also wishes to know whether the spleen increases in function or enlarges after stimulative doses of the roentgen ray. He reports in detail the blood examinations before and after roentgen therapy, especially after application to the spleen.

Bottner[1] reports 2 cases treated by the roentgen ray. One was improved and the other so improved as to be considered cured. Time, of course, will be necessary to establish the permanency of this successful result.

Treatment by venesection gave excellent results in the case reported by Richards.[2] There was an improvement, clinically, as well as in the blood count. The subjective sensations of headache, dizziness, tingling and numbness almost entirely disappeared after the first venepuncture. Altogether nine venepunctures were performed, the last eight chiefly in the hope of influencing the red cell count. After the first venepuncture the red cells dropped 2,000,000 and the hemoglobin from 115 to 96 per cent.

Pernicious Anemia. It is still unsettled as to how this severe anemia is brought about, whether abnormal destruction or defective hemopoieses, or both, are at fault. As one writer[3] points out, the invariable presence of large quantities of iron in the organs of patients dying from pernicious anemia suggests that an abnormal destruction of erythrocytes is an important factor in the production of the anemia, but it is not a proof of the presence of a hemolytic toxin; it may merely mean that unhealthy cells are produced by the bone marrow. The presence of megaloblasts in the blood stream in pernicious anemia points to a pathological condition of the marrow, for the small normoblasts rather than the large nucleated forms are characteristic of normal regeneration, and the neutrophile leucopenia so commonly seen in this disease is further indication that the hemopoietic system is at fault. Throughout life the cells of the blood, in common with almost all the other cells of the body, are constantly dying and being replaced, and the hemopoietic tissues possess such remarkable powers of compensation that a considerable destruction or loss of blood is possible without there being more than a transient anemia. Nevertheless, it is conceivable that a

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[1] Deutsch. med. Wchnschr., 1921, **47**, 773.
[2] Minnesota Medicine, 1921, **4**, 161.
[3] Lancet, 1921, **200**, 979.

perfectly healthy bone marrow may be unable to cope with the calls made upon it by abnormal continued blood destruction, with the result that a recognizable anemia occurs. More commonly, however, the deleterious agent which destroys the cells of the circulating blood acts also upon the marrow, so that there is both abnormal destruction and defective regeneration.

Ashby[1] is of the opinion that there is no hemolytic toxin producing the anemia in pernicious anemia. Partial evidence is presented to show that the periods of active blood destruction which are seen as the exception in pernicious anemia cases during a series of transfusions are due to the activity of the blood-destroying organs of the body rather than to the intrinsic weakness of the pernicious anemia blood corpuscle.

The influence of such agents as roentgen ray, radium, T. N. T. and arsphenamine in the production of severe anemias approaching in some instances the aplastic type is reported by Williams.[2] Mottram[3] and Moore and Keidel.[4] Williams believes that in the instances of T. N. T. and the gamma rays there occurs first a stimulation then an exhaustion from destruction of the marrow. Moore and Keidel state that aplastic blood changes with stomatitis and dermatitis are not of infrequent occurrence after arsphenamine. In illustration, they record the case of a woman, aged fifty years, suffering from primary syphilis, who, after a course of treatment during which 4.45 gms. of neoarsphenamine were administered, developed an ulcerative stomatitis accompanied by an extensive purpuric eruption. The blood showed on examination an aplastic anemia with marked diminution of red cells, a severe leucopenia, and a reduction of the platelets to 28,000 per c.mm. She died four weeks after the onset of the reaction. At necropsy there were extensive subcutaneous and subserous hemorrhages, hemorrhages in the stomach, intestines and liver, a hemorrhagic nephritis, and an aplastic bone marrow. Microscopical sections, examined by McCallum, showed that the bone marrow of the femur consisted almost entirely of fat; there were, however, a number of cells having large, rounded, eccentric nuclei, and a purple non-granular cytoplasm, with an area of pale staining around the nucleus resembling plasma cells, which were also met with in the splenic reticulum and the connective tissue of the liver. These he was inclined to regard as the basophilic ancestral cells of myelocytes. Large areas of necrosis were encountered in the liver. These authors express the opinion that the occurrence of itching, a mild macular or vesicular rash, prolonged fever, malaise, or any tendency toward purpura, accompanied by an alteration in the blood picture, are to be looked upon as the danger signals in treatment by arsphenamine.

Two cases of *pernicious anemia with infective foci* in the alimentary tract are reported by Maynard and Sturton.[5] There was a history of colitis in the first case and of diarrhea in the second. In the first case a definite ring of ulcers was found in the intestine, and in the second

[1] Journal of Experimental Medicine, 1921, **34**, 147.
[2] Lancet, 1921, **201**, 74.
[3] Archives of Radiology and Electrotherapy, 1920, **25**, 197.
[4] Archives of Dermatology and Syphilology August, 1921.
[5] British Medical Journal, 1921, **2**, 685.

an infective focus in the teeth. The first patient died, the second has apparently recovered under novarsenobillon and vaccines. Time only will tell whether this is a genuine recovery or a remission. Coda[1] records 2 cases of pernicious anemia in malarial subjects, aged forty-two and fifty-six years respectively. The blood picture in the first case showed hemoglobin 20 per cent, red cells 650,000, color index 1.5, leukocytes 3000, pronounced poikilocytosis, anisocytosis, megalocytes, polychromasia and megaloblasts. There were also anorexia, diarrhea, and achylia gastrica. In the second case, in which achylia gastrica was also present, the red cells numbered 1,200,000, the leukocytes 4000, hemoglobin 35 per cent, color index 1.4. There were also anisocytosis, anisochromia, a few normoblasts, megaloblasts, and myelocytes. Recovery took place in both cases under quinine treatment.

Clinical Studies. A clinical study was made by Levine and Ladd[2] of 150 consecutive cases, with special reference to gastric anacidity. The gastric function was analyzed in 107 of the 143 cases of pernicious anemia. In only 3 cases was free hydrochloric acid found at any time in the gastric secretion, and in 2 of these cases the diagnosis of pernicious anemia was questioned. These figures, then, show a persistent anacidity in 104, or 99 per cent of cases of pernicious anemia. A distinct familial incidence was discovered in 9 patients. Syphilis bore no relation to the development or course of pernicious anemia in this series. Of 143 patients, 6, 4.3 per cent, gave a positive Wassermann, which is about one-third the percentage of positive Wassermann reactions in all medical patients admitted to the hospital. When the Wassermann reaction was positive, antisyphilitic treatment did not alter the course of the anemia. The presence of eosinophilia is a common finding in pernicious anemia. Out of the 143 patients, 54 showed 5 per cent or more at one time or another. Even a very high eosinophilia—25 per cent or more—is not incompatible with the disease. In 76.9 per cent of the cases, the blood smear might be called typical of pernicious anemia, in 18.2 per cent it was suggestive, and in 4.9 per cent it was atypical or within normal limits. This is in striking contrast with the more constant finding of anacidity. Of 127 patients in whom the appearance of the tongue was described, in 63.8 per cent it was typically smooth and atrophic, in 19.7 per cent it was suggestive, and 16.5 per cent its appearance was about normal. Notwithstanding the fact that this disease belongs to adult age, the hair seems to turn gray prematurely and often takes on a strikingly silky white appearance.

The *spinal cord changes in pernicious anemia* are not infrequent and occur often rather late in life, according to Wilson and McIver.[3] The onset of the disease is gradual, and the symptoms are much the same in every case. Paresthesia in the hands and feet has been an early and constant complaint, and with this goes a gradual increasing weakness, more marked in the lower extremities.

[1] Il Policlinico Sez. Med., March 1, 1921; abstract, British Medical Journal, 1921, Epitome, June 18, 97.
[2] Johns Hopkins Hospital Bulletin, 1921, **32**, 254.
[3] Pennsylvania Medical Journal, 1921, **25**, 189.

The characteristic motor and sensory losses are as follows: The lower limbs show the signs of pyramidal tract involvement with the loss of the sense of position and of vibration. The other forms of sensation remains intact until late in the disease. The spinal cord symptoms are frequently present when the blood picture is almost normal. This is due to the toxin which, in many cases, causes spinal cord degeneration before the blood is affected. Schneider[1] states that in 80 per cent of all cases of pernicious anemia, there will appear, sooner or later, objective findings in one or more of the following fields: (1) loss of vibration sense in the distal ends of the long bones of the limbs, particularly; (2) loss of position sense, or joint sense, with, or without, loss of vibration sense; (3) loss of tactile-sense to cottonwool in fingers and toes; (4) motor disturbances, with ataxia and loss of the deep reflexes.

Meninger[2] reports a case in which the spinal cord symptoms were more conspicuous and antedated the anemia. The patient was a man, aged sixty-two years, who developed symptoms of ataxic paraplegia at fifty-five years of age and pallor at sixty years of age. Hamilton and Nixon[3] report a study of the sensory changes in the subacute combined degeneration of pernicious anemia. Feelings of deadness in legs, muscle insensibility, girdle sensations, loss of touch, hyperesthesia, etc., are among the recorded symptoms. Among 10 patients with subjective sensory disturbance, 8 showed loss of vibration sense over several or more bony prominences; 7 showed definite involvement of position sense in the toes; 7 showed diminished or absent tactile sensation in some areas. The subjective sensory disturbances constitute the earliest evidence of involvement of the nervous system which with the objective signs often form the earliest evidence of pernicious anemia. Degenerative changes in the peripheral nerves are common and constitute an important part of the pathological anatomy of the disease. Brandes[4] states that among those patients in which the spinal cord symptoms occur early in the course of pernicious anemia the diagnosis of the latter condition is most difficult. In the neurological examination particular attention should be paid to carrying out the sensory tests, especially for vibration and joint sensation. As approximately one-third of the cases of combined scleroses are due to pernicious anemia, it is always well to keep in mind this latter condition.

The TREATMENT OF PERNICIOUS ANEMIA is summed up by Osborne[5] as follows: (1) If a Wassermann test is positive, administer arsphenamine. (2) Seek, and, if found, remove parasites from the intestines. (3) Seek, and, if found, remove focal infections. (4) Prevent putrefaction in the intestines. (5) Colon washings may be of value. (6) Administer hydrochloric acid, small amounts of iron, not infrequently a small daily dose ($\frac{1}{4}$ to $\frac{1}{2}$ grain) of thyroid, and a fair daily dose (1 to 2 grains) of suprarenal. The suprarenals are generally insufficient in

[1] Southern Medical Journal, 1921, **14**, 442.
[2] New York Medical Journal, 1921, **113**, 812.
[3] Archives of Neurology and Psychiatry, 1921, **6**, 1.
[4] Minnesota Medicine, 1921, **4**, 564.
[5] New York Medical Journal, May 18, 1921, 721.

any infection or chronic disability. Mild thyroid stimulation is frequently indicated. Preparations of red bone marrow are of value. (7) The rest of the treatment consists of sunlight, fresh air, good food, and perhaps heliotherapy. Biffis[1] points out that diarrhea, when it occurs, may perhaps be due to deficiency of HCl in the gastric juice, for it may often be relieved by administering HCl by the mouth.

Giffin and Szlapka[2] have published the results of splenectomy in 50 cases in which the immediate operative mortality of the series was 6 per cent. Forty-two of the 47 patients who recovered from operation have died. Ten (21.3 per cent) lived longer than three years, while 21 (45 per cent) lived longer than eighteen months after operation. Five (10.6 per cent) of the 47 patients who recovered from operation are alive; 2 were splenectomized four years and nine months ago, 1 four years and eight months, 1 four years and five months, and 1 four years and three months. These 5 patients, at the time of their last reports, were in good general condition. Including with these the patients who survived operation at least three years but who are now dead, there is a total of 10 (21.3 per cent) in whom the total duration of disease before and after operation was four and a half years or more. This is clearly longer than the average expectation of life of patients with pernicious anemia, and would seem to lead to the definite conclusion that life is prolonged in a considerable percentage of cases.

Upon neurological examination before operation, 29 patients (58 per cent) showed definite evidence of sclerosis of the spinal cord. Eight more (16 per cent) registered complaints suggestive of early involvement of the spinal cord, making a total of 37 patients (74 per cent). Marked degeneration of the cords has not progressed in patients in whom the degeneration was slight previous to splenectomy. It is possible that the progress of the degeneration is arrested in some of the patients. Mental symptoms have not developed following operation. In the selection of patients for operation in this series, preference was given to persons between the ages of thirty-five and forty-five years, with a previous history of one year or less, a favorable type of blood-picture, and with little if any evidence of degeneration of the spinal cord. An absence of marked leucopenia with a polymorphonuclear rather than a lymphocytic predominance in the leukocyte count, marked hemolytic activity, estimated by the examination of the pigments in the duodenal contents, in the presence of a competent bone marrow and a moderately enlarged spleen, were regarded as favorable to splenectomy. Patients in acute exacerbations and patients showing evidence of bone marrow exhaustion were excluded so far as possible.

Blood transfusion has been regarded as a procedure favoring the occurrence of a remission in patients with pernicious anemia. That it has lengthened life in many instances, cannot be doubted. That repeated transfusion is not without danger is illustrated by the experience of Bowcock.[3] In 3 cases which he reports, serious reactions occurred

[1] Policlinico, June 27, 1921.
[2] Journal of the American Medical Association, 1921, **76**, 290.
[3] Johns Hopkins Hospital Bulletin, 1921, **32**, 83.

after repeated transfusions of apparently compatible blood. In 2 of these cases the severity of the reaction seems to have been largely responsible for the death of the patient. It was considered inadvisable and dangerous to continue this form of therapy in the other patient, who died a short time after discharge from the hospital. Bowcock concludes that our present methods are inadequate for selecting suitable donors for some cases of pernicious anemia which have been repeatedly transfused. In other words, in certain patients suffering from pernicious anemia, who have been transfused repeatedly, transfusion becomes self-limited because of the inadequacy of methods for selecting suitable donors. This difficulty having once been discovered, no attempts should be made to transfuse these patients. The severe reaction is probably due to an anaphylactic manifestation, and not to hemolysis *per se*. Blood-matching should be carried out with the greatest care; whenever possible, the incubation period should be at least two hours, or longer. Members of Group IV cannot be regarded absolutely as universal donors.

An interesting study on germanium dioxide as an erythropoietic agent is reported by Hammett and Nowrey.[1] This substance is without toxic effect when used in white rats and produces in these animals, following injection, an increase in the red cells without an effect on the white cells. The liver and bone marrow show changes indicative of the action of germanium dioxide on these parts. It is to be hoped that further studies will reveal its non-toxic effect in man and its value in diseases of the blood-forming organs that result in anemia.

The Blood in Acute Nitrobenzol Poisoning. Nitrobenzol, or oil of mibrane, is a coal-tar derivative having the appearance of a pale yellow liquid which smells and tastes like oil of bitter almonds. Nitrobenzol is employed in the manufacture of high explosives and is used to a limited extent in perfumery, soap, confectionery and cookery processes, in making dyes, and in pharmaceutical laboratories. It is remarkable that a poison which is put to so many commercial uses should not be more toxic to people who handle it constantly.

Loeb, Bock and Fitz[2] report 2 cases of acute nitrobenzol poisoning, with blood studies. Both patients were young men who were poisoned by drinking Jamaica ginger which was subsequently analyzed and found to contain a high percentage of nitrobenzol. The clinical history is as follows: In about three hours after beginning to drink, one man began to have generalized headache, nausea and blurring of vision. He thought that he fell on the sidewalk and remembered nothing further until he woke up in the hospital. The other man, at about the same time, began to feel dizzy and nauseated. He did not lose consciousness, but came to the hospital with his friend. At entry, both men were of a steel-gray-blue color, the unconscious man looking practically dead, while his companion was of a ghastly color but in reasonably good shape. There was nothing else especially notable except that

[1] Wistar Institute Abstracts, 1921, Journal of the American Medical Association, 1921, **77**, 1578.
[2] American Journal of the Medical Sciences, 1921, **161**, 539.

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neither man excreted any urine for at least six hours after entry to the hospital. The stomachs of both men were washed out at once. The sicker man was bled 100 cc of blood and transfused with 600 cc of normal blood. In the middle of transfusion, he suddenly woke up and appeared normal. The second man was also transfused, but with less dramatic effect. Both men, however, felt perfectly well on the following day and made normal recoveries, except that the more seriously poisoned man developed a mild, uncomplicated pneumonia.

The blood studies were quite interesting. The oxygen capacity of both bloods on the first observation was markedly reduced, in 1 case being only 6.2 volumes per cent. The total hemoglobin was not reduced. The fact that methemoglobin was not detected by spectroscopic examination suggests that a large proportion of the hemoglobin was changed to nitrobenzol hemoglobin. This combination, in turn, was an easily destroyed compound, as demonstrated by the blood analysis made twenty-four hours later. By this time the appearance of both patients was much more nearly normal, and the bloods showed no diminution in their total hemoglobin, oxyhemoglobin or oxygen capacity. All cases, however, do not react this way, as many have been reported with unquestioned methemoglobinemia. Although it so happens that the cases of nitrobenzol poisoning recently reported have been mild, they often present a serious and not infrequently fatal condition.

The following fatal case, occurring some years ago at the Massachusetts General Hospital, is quoted by Loeb, Bock and Fitz: The patient, a man, aged forty-five years, was cleaning a railroad car with fluid which contained nitrobenzol. In some manner he broke the container so that its contents spilled over the lower half of his abdomen, soaking his clothes below the thorax. When he reached the emergency ward of the hospital, approximately forty-five minutes after the accident occurred, he was totally unconscious, intensely cyanosed and died in a short time. The impressive fact in relation to this case was that nitrobenzol absorbed through the skin caused death within almost a few minutes after exposure.

Paterni[1] reports a case of nitrobenzol poisoning from suicide intent. Dimness of vision was the first symptom, then dizziness, vomiting and total blindness, followed by cyanosis, spasms, and coma. About the sixth day jaundice appeared, the red cells dropping to 2,600,000 by the ninth day. By the thirteenth day most of the severe symptoms had cleared up, although the red cells still numbered only 2,500,000. The treatment consisted of gastric lavage, camphor and caffein hypodermatically, oxygen inhalations and external heat.

Hamilton,[2] from investigations upon 402 workers engaged in T. N. T. works, concludes that the poison is absorbed chiefly through the skin, and that avoidance of direct contact, cleanliness of the premises, clothes, socks and gloves, and the provision of ample washing facilities are necessary for prevention. Though fumes may cause poisoning, they

[1] Policlinico, 1921, **28**, 353.
[2] Journal of Industrial Hygiene, July, 1921.

alone probably never cause the more serious forms. The young appear to be more susceptible than adults. The Webster test for the urine showed that T. N. T. is rapidly absorbed, but it also rapidly eliminated, the urine becoming free from the reduction product in from twelve to twenty-four hours; hence the value of week-end holidays and of occasional suspensions from work. Though this test does not as yet aid in diagnosis, the color changes in untreated urine and the blood changes found are of sufficient significance to lead to further investigation with this end in view.

In those cases in which the anemia is of a severe type, no parallelism could be established between its occurrence and that of toxic jaundice, according to O'Donovan.[1] The jaundice is probably the result of a toxic action on the liver cells.

The Leukocytes. THE LEUKOCYTES AFTER EXPERIMENTAL HEMORRHAGES were studies by Musser[2] in the course of some experiments on blood regeneration after simple anemia. Eight dogs were used in the experimental work. After bleeding, they were placed on a standard diet and systematic blood-count observations recorded. As a result of these studies, Musser concludes that a marked leukocytosis is the general but not constant rule after hemorrhage, and is of variable duration. The persistence of the leukocytosis would seem to bear a general relation to the severity of the hemorrhage. This leukocytosis is made up largely of an increase in the polymorphonuclear neutrophiles. Eosinophiles do not disappear from the circulating blood as they do in the leukocytosis of sepsis and other conditions. The factors which seem to play a part in the pathogenesis of the condition are: Retention of the leukocytes in the blood stream during hemorrhage by adhesion to the vessel walls, with diminution of blood volume, and, presumably, an outpouring of white cells from the bone marrow after hemorrhage in response to an unknown stimulus.

The *leukocyte count* may be of diagnostic significance *in* the differentiation of *carcinoma and achylia gastrica*, according to Weinberg[3] who found in 68 cases of carcinoma a normal leukocyte count in 26 patients, leukocytosis in 27 patients and leucopenia in 15 patients. Among 67 patients with achylia, a normal leukocyte count was found in 37 patients, leukocytosis in 7 patients and leucopenia in 23 patients. In the light of these observations, leukocytosis must therefore be regarded as pointing to carcinoma rather than achylia. In the differential count, however, lymphocytosis was rather indicative of achylia and lymphopenia pointed to carcinoma.

The LEUKOCYTES IN INFLUENZA were studied by Bunting[4] who found a rather characteristic blood picture. The features of this are an early neutrophile leukocytosis followed by a sharp drop to leucopenia, with a marked deficiency in cells of marrow origin and of blood platelets and with a lymphocytosis of varying degree. There is a gradual return

[1] Editorial, British Medical Journal, 1921, **1**, 395.
[2] American Journal of the Medical Sciences, 1921, **162**, 40.
[3] Deutsche medizinische Wochenschrift, 1921, **47**, 826.
[4] American Journal of the Medical Sciences, 1921, **157**, 1.

toward a normal picture, but a cessation of fever and of symptoms may occur with the presence of a very abnormal blood count. The leuco-penia suggests somewhat that of typhoid fever, and also somewhat that of measles. It indicates sharply that the primary infecting agent is not a pyogenic coccus. The leucopenia in influenza would appear to depend upon a marrow inhibition like that in typhoid fever, and not upon a severe injury to the marrow or to its exhaustion, for in both diseases, given a pyogenic stimulation of the marrow through secondary infection, there is immediate response with a neutrophile leukocytosis, at least in reactive individuals. The nature of this marrow inhibition or negative chemotaxis is not evident. The great poverty in circulating neutrophilic leukocytes would seem to account for the frequency of pyogenic complications in influenza. The great platelet decrease is apparently responsible for the hemorrhagic character of the pneumonic exudate in that complication of the disease.

The EOSINOPHILE LEUKOCYTES in the blood of 40 patients with CHOREA were found to average 7.6 per cent., according to Berger.[1] The highest count was 26 per cent and the lowest 0. Among 55 patients with *scabies*, Hayman and Fay[2] found eosinophilia of 5 per cent or more in 32 patients, or 58 per cent. In approximately 37 per cent the eosinophilia exceeded 7 per cent. The degree of the eosinophilia was, in general, proportional to the extent of the infestation.

The LEUKOCYTE COUNT IN EPIDEMIC ENCEPHALITIS, according to Neal,[3] who had an experience with more than 100 cases in children, varies from normal to one showing a moderate degree of leukocytosis, perhaps up to 15,000 or 20,000.

THE FATE OF THE LYMPHOCYTE is the subject of an interesting paper by Bunting and Huston[4] which called forth two editorial[5] comments. It has been estimated that more lymphocytes enter the blood in the course of a day than can be found in the blood at any given time. What becomes of these cells is the natural question. According to Bunting and Huston, this excess of lymphocytes is not destroyed in the blood stream. The cells migrate from the bloodvessels into the mucous membranes and through them to their surface. This occurs chiefly in the gastro-intestinal tract, and it is apparently in the mucosa, and especially within the intestinal lumen, that the function of the lymphocyte is normally performed. What this function may be is unknown, but the immunity of the gastro-intestinal mucosa to the countless bacteria and their toxins within its lumen suggests the possibility that the lymphocyte may affix toxins. As pointed out editorially, the lymphocytes are not phagocytic, so that they can scarcely be conceived to protect the body by engulfing microörganisms. Whether they are responsible for some degree of immunity to harmful chemical products, or act in some quite different local physiologic function, remains to be ascertained. In

[1] American Journal of Diseases of Children, 1921, **21**, 477.
[2] Archives of Dermatology and Syphilology, January, 1921.
[3] Journal of the American Medical Association, 1921, **77**, 121.
[4] Journal of Experimental Medicine, 1921, **33**, 593.
[5] Journal of the American Medical Association, 1921, **76**, 1769, and British Medical Journal, June 28, 1921, 905.

any event, if the cells migrate from the bloodvessels into the mucous membranes and through them to their surfaces, as has just been reported, the reason for this remarkable behavior demands earnest consideration.

Leukemia. It has been recognized for some time that the diagnosis of the type of leukemia, that is, lymphocytic or myelocytic, is often difficult from a consideration only of the clinical data and blood smears stained in the usual way. The statement that in lymphatic leukemia the lymph glands are enlarged out of proportion to the spleen, and in myelogenous leukemia the splenic enlargement is more prominent, is true only in a certain number of cases. The blood smear, while more accurate, is in a measure uncertain too in the type diagnosis, for there are many questions among observers in regard to differentiation between lymphocytes and myelocytes. The simple statement that the myelocytes are granular and the large lymphocytes non-granular is a good working foundation, but the difficulty is in the recognition of the granules by the ordinary methods of staining.

As Lambright[1] points out, the best plan is to stain all blood smears from leukemia patients by the oxydase method. In the use of this method, to quote Lambright, alpha-napthol and dimethylpara-phenyl-endiamine are brought together in the presence of an oxidizing agent which is present in the leukocytes. An alkaline media is required. When this is done a rapid precipitation of indophenol blue occurs which produces blue granular staining of their protoplasm. The reaction is given by neutrophil, eosinophil and basophil leukocytes and by myelocytes in bone-marrow and leukemic blood. The reaction is not given by lymphocytes nor red blood cells. The method is as follows. Solutions required:

SOLUTION A.

95 per cent alcohol	9 parts
Formaldehyde solution (40 per cent gas)	1 part

SOLUTION B.

Alpha-naphthol (Merck's reagent)	1 gram
40 per cent alcohol	100 cc
Hydrogen peroxide	0.2 cc
(Must be fresh.)	

SOLUTION C.

Pyronin	1 gram
Anilin	4 cc
40 per cent alcohol	96 cc

SOLUTION D.

0.5 per cent solution of methylene blue (Grubler's BX).

The films should be fixed by covering with solution A. After two minutes this is washed off with water and film flooded with solution B. This is washed off and the film is allowed to remain in a dish of running water for fifteen minutes. It is then dried and stained for two minutes with solution C. This is washed off with water and solution D is

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[1] American Journal of the Medical Sciences, 1921, **161**, 209.

poured on and allowed to remain for thirty to sixty seconds. After washing with water, the slide is blotted and mounted in neutral balsam.

Lambright refers to a leukemia patient whose blood was studied in the ordinary way by three hematologists. In two instances the report came back as myelogenous leukemia, and in one lymphatic leukemia. The oxydase method was of real value in establishing the type diagnosis in this patient.

Aleukemic leukemia, or leukemia with a normal or only slightly abnormal cell count, offers another diagnostic difficulty. Blankenhorn and Goldblatt[1] state that, out of 52 leukemic cases, 6 had a normal count some time during observation and 3 of the 6 never had an abnormal leukocyte count. In the great majority of cases the diagnosis must depend upon the finding of either an abnormal count or abnormal cells some time during the course of the disease. Paisseau and Alcheck[2] describe an *acute aplastic leukemia* in a patient in whom the leukocytes showed only a transient increase, the blood picture differing from that in pernicious anemia only by the appearance of undifferentiated cells; 84 per cent of the leukocytes were of the embryonal type. The symptoms were those of septicemia, with severe pains in heel and calf, suggesting gonococcus septicemia; later, delirium, muscle rigidity and intense pains in the bones were features. The entire skeleton was tender; the woman screamed when the sternum, ribs and tibias were even touched. Death occurred in three months.

It is in the acute types of leukemia that abnormal cells present difficulties in classification. As Fiessinger and Broussole[3] state, these cells are young cells thrown into the circulation before complete differentiation has had time to occur. The cell is mononuclear and nongranular, resembling in some respects a large lymphocyte, but differing from it in that it is much larger, that its nucleus is often oval or indented, that its chromatin network is less dense, that one or more nucleoli are frequently present, and that occasionally at one side of the nucleus only there is to be made out a fine area of basophile protoplasm.

In reviewing the literature with regard to the occurrence of this undifferentiated cell in acute leukemia and its differentiation by biologic methods, *i. e.*, the proteolytic and oxydase reactions, these same authors found 22 cases in which, by means of the proteolytic reaction, 12 were positive and 10 negative; while of 55 cases in which the oxydase reaction was used, 29 were positive and 26 negative. In 3 cases of their own both reactions were negative.

Acute leukemia of either lymphatic or myelogenous type is a serious and rapidly fatal disease as a rule. In Villela and Torris's[4] patient, a man, aged twenty-eight years, the acute leukemia of a myelocytic type ran a rapidly fatal course with death in less than three weeks. As a rule, the acute lymphatic leukemia is the more rapid of the two types.

[1] Journal of the American Medical Association, 1921, **76**, 583.
[2] Bulletins de la Société Médicale des Hôpitaux, 1921, **45**, 1424.
[3] Annals de Med., August, 1921; abstract, British Medical Journal, October 29, 1921, 64.
[4] Brazil-Medico, 1921, **1**, 327.

The *symptoms of acute leukemia* are recalled to us again by Whitcroft's[1] paper. A rapidly advancing pallor and weakness or severe hemorrhage may be the first indications of the disease. Irregular fever, often with great sweating, thirst and anorexia, vomiting, diarrhea, repeated hemorrhage from nose, gums, bowels, and subcutaneous extravasations are among the usual symptoms during the course. Enlargement of the lymphatic glands is sometimes well marked, especially in the lymphatic form, and may be one of the earliest symptoms noted by the patient. Among other early symptoms is angina, often of an ulcerative character involving the tonsils and pharynx. Kaltenbach[2] records a fatal case of acute leukemia in a man, aged thirty years, in whom death occurred suddenly owing to edema of the glottis secondary to ulceration of the epiglottis after three weeks' illness. Splenic enlargement is usually slight in the acute form, and the spleen, as in any acute condition affecting it, is more likely to be soft than in the chronic form. The lymphatic glands are usually enlarged but usually moderate in extent and may even be absent. The cervical glands are the most frequently implicated, and the enlargement may be limited to them or may extend to axillary, inguinal and mesenteric glands. Disturbances of the alimentary system are common. The tonsils and lymphoid tissue may be so enlarged as to give trouble in swallowing, especially when this is complicated by inflammation, which frequently occurs. In many acute cases the chief early symptoms are related to lesions of the mouth. These are due to swelling of the tissues from lymphocytic deposits and also to infective processes which supervene. The gums may become much enlarged, spongy, inflamed, and bleed easily; the teeth may become loosened and the proper closing of the mouth be interfered with. There is often decomposition of blood and marked fetor. The tissues are easily injured and necrosis and ulceration, or even gangrene, may occur. The term leukemic stomatitis has been applied by Mosler to this condition. Sabrazés[3] states that acute leukemia may simulate septicemia, typhoid fever, dysentery, acute or subacute pulmonary tuberculosis, purpura hemorrhagica, scurvy, acute rheumatism, or acute nephritis. Sometimes the disease is complicated from the first by hemorrhagic and gangrenous processes in the pharynx, buccal mucosa, or gums, so as to resemble hypertoxic diphtheria, or noma. Lastly, the disease may be mistaken for acute meningitis, because of meningeal hemorrhage, or for urticaria pigmentosa because of leukemic lesions of the skin.

In contrast to this fatal disease is the benign condition which has been reported by Bloedorn and Houghton,[4] in which during an acute infection, usually of the tonsils or upper respiratory passages, abnormal leukocytes appear in the blood and give rise to a blood picture strikingly similar to acute lymphatic leukemia. However, the total white count never became so large that it could not be accounted for as the result

[1] Pennsylvania Medical Journal, May, 1921, 567.
[2] Arch. des mal. du cœur, April, 1921.
[3] Gaz. hebd. des Sci. Med. de Bôrdeaux, March 6 and 13, 1921.
[4] Archives of Internal Medicine, 1921, 27, 315.

of reaction to acute infection; there was no hemorrhagic tendency and no degenerated or fragile cells were noted in the smears. The predominating type of cell was the lymphoblast, and the Reider type of lymphoblast was frequently noted. All of these cases showed enlargement of the lymphatic glands, particularly the cervical and submaxillary glands. They all pursued a benign course and ended in complete recovery. The term *acute benign lymphoblastosis* is suggested as covering this type of case.

Enlargement of the lymphatic glands with lymphocytosis is not of infrequent occurrence. Last year we had occasion to refer to the report of Sprunt and Evans[1] whose 6 cases were not unlike those of Bloedorn and Houghton. Sprunt and Evans referred to their patients as instances of *infectious mononucleosis*. All of their patients likewise recovered. An editorial[2] comment on infectious mononucleosis and benign lymphoblastosis points out that these cases have been recognized in the past under the name of glandular fever.

Leukemia in children, with special reference to lesions in the nervous system, is described by Bass.[3] Among 23 cases, for the most part acute types, 6 presented prominent symptoms referable to the nervous system. Four of these gave the picture of cerebral hemorrhage. Three were proved cases; 1 by postmortem examination, 2 by lumbar puncture. The fourth case neither came to necropsy nor had a puncture performed; from its clinical picture, however, cerebral hemorrhage could with probability be diagnosed. The fifth case at first was mistaken for cerebrospinal meningitis, the clinical findings pointing to a leukemic infiltration as the cause of the symptoms. A similar case with necropsy is reported from the literature. The sixth patient had terminal cerebral symptoms and macroscopic leukemic infiltration was found at postmortem examination.

Bass refers to the work of Tapie and Cassar,[4] who comment on the fact that leukemic infiltration of the nervous system may be present without causing any symptoms whatever. In their article, which contains a very good review of the literature bearing on this subject, they report a case of hemiplegia due to capillary hemorrhage and leukemic infiltration of the internal capsule. They classify the nervous lesions which may occur in leukemia under the following heads:

1. Medullary degeneration: Small foci of sclerosis or capillary hemorrhage in the brain or cord.
2. Leukemic infiltration: This may or may not cause symptoms.
3. Hemorrhages in nerve centers.
4. Nerve lesions due to compression.
5. Zoster.

Harris'[5] patient, a youth, aged seventeen years, with lymphatic leukemia, presented an early well-marked polyneuritis. The polyneuritis was symmetrical and appeared before the definite diagnosis of the blood

[1] Bulletin of Johns Hopkins Hospital, 1920, **31**, 410.
[2] British Medical Journal, January and April, 1921, 95 and 649.
[3] American Journal of the Medical Sciences, 1921, **162**, 647.
[4] Arch. de mal. du cœur, 1919, **12**, 218.
[5] Lancet, 1921, **200**, 122.

condition was possible to establish. The polyneuritis, according to Harris, was a toxic manifestation and not due to leukemic infiltration. To date, so far as he could ascertain, no like instance has been recorded.

As *an aid to the diagnosis of leukemic infiltration of the leptomeninges,* Barker's[1] experience will bear remembering. In 1 case he was able to demonstrate in the cerebrospinal fluid the presence of cells of leukemic origin (myelocytes and, perhaps, myeloblasts). In no other case thus far reported has the presence of leukemic cells in the cerebrospinal fluid during life been described. In the few instances in which lumbar puncture has been done in leukemia, the cerebrospinal fluid has been negative, or has merely shown a trace of blood or an increase of globulin. The presence of cells of leukemic origin in the cerebrospinal fluid probably indicates a leukemic infiltration of the leptomeninges.

Skin manifestations in the leukemias are fairly common, especially in the late stage when the disease becomes hemorrhagic and petechiæ appear. Many other lesions have been described—none so frequent or so characteristic as petechiæ—but they are all said to be of a common pathology, and when studied in section should be very useful in the diagnosis of leukemia. Blankenhorn and Goldblatt[2] report an interesting case of lymphatic leukemia in which the skin lesions were the most conspicuous symptoms of the disease. Their patient, an adult male, lacked the familiar blood picture, lymph-node enlargement and tendency to hemorrhages. When admitted to the Lakeside Hospital the entire surface of his body, including his scalp, the soles of his feet and the palms of his hands, was covered with very striking skin lesions. These were of various kinds and shapes, ranging from miliary points to patches more than 5 cm. in diameter. The majority of them were purple, hemorrhagic in appearance, and slightly elevated, thick and firm. Some of the lesions showed only extreme reddening, while in others there was a purple that had faded to a brown. Some of them were desquamated with a brown dry scale, while others had superficial layers elevated by a sticky layer of creamy pus. None were deeply ulcerated, and all showed varying stages and degrees of infiltration and hemorrhage. In particular, no single lesion could be said to be a simple purpura unaccompanied by infiltration. The membranes of the mouth and conjunctivæ showed the same lesions, but here superficial ulceration, complicated by secondary infection and encrusting, was more marked. Two sections of skin were studied microscopically but no definite diagnosis was made. The opinion rendered was probably leukemia or lymphosarcoma. Subsequently at necropsy sections of various organs were obtained and leukemic infiltration, lymphatic type, of skin, heart, right lung, kidneys, pancreas, liver, thoracic lymph nodes and abdominal lymph nodes was demonstrable.

MICROLYMPHOIDOCYTIC LEUKEMIA. Fineman[3] reports a case of leukemia in which the blood contained enormous numbers of cells, which ordinarily would be called "the rare micromyeloblasts." The

[1] Southern Medical Journal, 1921, **14,** 437.
[2] Journal of the American Medical Association, 1921, **76,** 583.
[3] Archives of Internal Medicine, **29,** 168.

blood picture was like that of myelogenous leukemia. Clinically, however, there was evidence pointing to lymphopoietic activity, namely, a mediastinal tumor, as revealed by percussion and roentgenograms, a very marked enlargement of lymph nodes over the entire body, and a markedly enlarged spleen. That the lymphopoietic organs were very active was proven by the sections of a lymph node, which showed that the blood cells referred to as "micromyeloblasts" were in reality proliferating right in the lymph follicles and germ centers of the node, and could be traced entering the circulation from the lymph node.

The case report is of interest because it offers strong evidence in favor of the unitarian theory of the origin of white blood cells. The history in brief is that of a girl, aged seventeen years, who came to the hospital complaining of weakness and rapidly enlarging masses in the neck and axillæ. She stated that she had been well up to four weeks prior to admission to the hospital. A physical examination revealed moderate fever (100.6° F.); pulse, 146; marked anemia; no edema, cyanosis, or jaundice. The neck and sides of face appeared swollen with irregular-shaped subcutaneous masses. Tenderness was present over frontal sinuses and mastoids and over left antrum. The eye-grounds showed extensive fresh hemorrhages. The gums were tender and bled on pressure. The tonsils were very large, glistening, pearly in appearance; so large that they almost occluded the entire pharynx. Chains and matted masses of glands were felt in the following regions: Anterior and posterior auricular; submaxillary; anterior and posterior cervical; left and right subclavicular; over both apices anteriorly and posteriorly; over the trapezii; in the axillæ and in the inguinal regions. These were all bilateral. They varied in size from that of a small pea to that of a hen's egg. Some were round; some were oval and many were matted. They were hard and not tender to pressure; were freely movable and not attached to the skin. The spleen was definitely palpable, 7 cm. below the costal margin in midclavicular line; the liver was not enlarged.

The patient was subjected to intensive clinical study during a period of about two and a half months, during which time numerous blood counts were made and twelve transfusions performed. The hemoglobin and red blood cell count remained low throughout, and both progressively diminished in spite of twelve transfusions, a total of 2760 cc of blood. The white cell count showed some extraordinarily sudden, unaccountable fluctuations. On entrance to the hospital, the patient's white cell count was 99,000. In twenty-four hours, before any treatment was instituted, the count fell to 44,000, followed by a further fall after roentgen ray exposure of the lymph nodes of the neck and mediastinum. From then on the white cell count kept oscillating between counts as low as 2300 and as high as 646,000 on the day of death. A very interesting finding, with counts over 80,000, was the presence of numerous mitotic figures in the blood. Nucleated red blood cells and myelocytes were present in small numbers.

The most interesting cell was the so-called "micromyeloblast" of Naegeli and Schridde, or the "microlymphoidocyte" or "stem cell"

of Pappenheim. The total number and relative per cent of this cell was practically directly proportional to the total count. With the rise in total white cell count the patient was always clinically worse and the disease could be said to have assumed a more severe aspect. Co-incidentally with the increase in the severity of the disease, the "micromyeloblast" would increase in number and percentage, a finding which is similar to the findings of Panton and Tidy in a series of 3 cases. With a white cell count of 2300, the total "micromyeloblast" count was 153. With a white cell count of 500,000, the "micromyeloblast" count rose to 75,000. On the day before death, the total white cell count was 646,000, but the "micromyeloblast" count was only 2548, probably an exhaustion phenomenon. The biopsy of a lymph node showed that at least a great number of "micromyeloblasts," a cell definitely myeloid according to the dualist view, were being generated in the germ center of the lymph node into the blood stream. Such a possibility has always been denied by the dualists.

Fineman points out that modern hematologists are divided into two strong groups, the so-called unitarians or monophyletists, on the one hand, and the dualists and polyphyletists on the other hand. The bone of contention between these groups is the so-called "stem cell." The dualists and polyphyletists consider the lymphopoietic and myelopoietic tissues as two separate tissues, entirely distinct from each other and never interchangeable. They contend that all the cells produced in lymphopoietic tissues come from their own specific stem cells, the "lymphoblasts," and in the same manner all cells produced in myelopoietic tissues come from their own specific stem cells, the "myeloblasts." They claim to be able to demonstrate a difference between "lymphoblasts and myeloblasts." The unitarian or monophyletists deny the specificity of "lymphopoietic" and "myelopoietic" tissues. They present admirable evidence that under certain conditions myeloid cells may be produced by "lymphopoietic" tissues, and, *vice versa*, lymphoid cells may be produced in "myelopoietic" tissues. Pappenheim and his followers claim that all blood cells spring from a single stem which they call "lymphoidocyte." While some unitarians do not admit that there is a morphologic difference between the "myeloblasts" and the "lymphoblasts," other observers grant such a possibility, but deny the specificity of the mother tissues from which these cells come. Reference was made in a previous paragraph to the oxydase reaction which the dualists claim is of prime importance in the differentiation of myeloblasts and lymphoblasts. It is positive in myeloblasts and negative in lymphoblasts.

Fineman points out that a vast amount of experimental evidence is accumulating, which is in favor of the unitarian theory, and refers to a number of cases in the literature favoring the unitarian viewpoint. He quotes Pappenheim as stating in 1912 that the unitarian theory will receive great support, and dualistic theory will receive a serious blow at the moment that a case would be found in which the so-called "myeloblasts" could be shown to originate from lymphatic tissue, that is, from the follicles and follicular cords. In others word, when in the blood

the cell morphology will be that of a "myeloblastic" leukemia, while the tissues will show lympholeukemic changes, *i. e.*, follicular hypertrophy and presence of myeloblasts within the lymph follicles. Fineman quotes Naegeli, who, in 1910, made the statement that under no circumstances has it ever been proven that the germinal center of the lymph nodes can act as the site of origin of myeloid cells. Fineman also refers to Citron's case (1915), which, from the blood picture and clinical findings, was diagnosed as "micromyeloblastic leukemia."

The postmortem histologic study showed that the bone marrow was entirely normal. However, the cells of the follicles, as well as the cells of the interfollicular tissue of the lymph nodes and spleen, contained a slightly enlarged, eccentrically placed, perfectly round nucleus which resembled very closely the nucleus of a "myeloblast." The largest forms, however, were not as large as those found in "myeloblastic leukemia." Fineman believes that the information which he obtained in his case to be more convincing than Citron's because the lymph node was obtained *in vivo*, so that postmortem changes can be ruled out. Citron speaks of "myeloblasts" and "micromyeloblasts" in the follicles, but he does not say that he found them in the germ centers. The germ centers in Fineman's case contained many of these cells. To summarize briefly, Fineman's morphologic studies:

The blood at all times showed numerous stem cells—lymphoidocytes of Pappenheim; myeloblasts of Naegeli—of all sizes. Morphologically these atypical stem cells were indistinguishable from typical myeloblasts. The oxydase reaction was negative in these cells in the blood smears. The diagnosis from the blood alone would be "micromyeloblastic" leukemia. The presence of numerous mitotic figures in the blood stream suggested the possibility of cell proliferation in the blood stream. Fineman could not demonstrate such to be the case. Lymphocytes, normal in appearance, were always present in the blood. The contrast between the lymphocytes and the atypical cells was very marked. Numerous transition forms between the lymphocytes and the atypical cells were present in the blood. Some myelocytes and nucleated reds were present. The severe anemia might easily account for these. The biopsy of a lymph node showed these atypical cells proliferating in great numbers in the capsule, interfollicular tissue, lymph cords, lymph follicles and in the germ centers of the lymph follicles. Transition forms between the connective tissue cells of the capsule and these atypical cells, as well as between lymphocytes and these atypical cells, were present in the capsule. In the interfollicular tissue as well as in the follicles and even in the germinal centers transition forms between these atypical cells and reticulum and lymphocytes were also present. The lymph follicles and lymph cords showed no signs of atrophy, but had all the earmarks of marked activity. Mitotic figures were numerous. The only signs of atrophy or necrosis were found in the capsule. These atypical cells formed the majority of the cells of the parenchyma. These atypical cells constituted by far the majority of the cells in the lymph sinuses and were very numerous in the blood-vessels of the node. From the evidence at hand, the conclusion is

justified that in all probability the majority of the "myeloblasts" and "micromyeloblasts" of the blood were coming from the lymphoid organs, not only from the portions which, according to the dualists, may give rise to myeloid cells, but from the sanctum sanctorum of the lymphoid tissues, namely, the follicles and germ centers.

TREATMENT OF LEUKEMIA. *Radium* and the roentgen ray continue as our most valuable remedies. *Splenectomy* is of qestionable value. Rénon and Degrais,[1] in a recent communication to the French Academy of Medicine, report that since 1910 they have treated 8 cases of leukemia by applications of *radium* to the spleen. Although all the patients ultimately died at dates ranging from two months to six and a half years after the commencement of treatment, the immediate effects were remarkably good. Spleens which had filled the whole of the abdominal cavity rapidly diminished from day to day under this treatment, and finally resumed their normal size. The number of leukocytes fell from 320,000 to 70,800, then to 20,000, 7000, and even lower. The myelocytes disappeared and the number of red cells increased.

The general condition improved, the fever subsided, the weight increased, and after four to six weeks' treatment a cure seemed to have been effected. Recovery, however, was more apparent than real, for from two to eighteen months after cessation of treatment signs of myeloid leukemia reappeared. Applications of radium were resumed, but with hardly any effect and death took place in a time ranging from two months to some years after the commencement of treatment. The occurrence of the relapses is attributed by Rénon and Degrais to progressive resistance of the myelocytes on which radium had no longer any effect, whether this was due to habituation of the myelocytes to radium like that of spirochetes to arsenic, or to a fibrous change in the leukemic spleen under the influence of treatment.

These same authors[2] report an instance of myeloid leukemia in which the patient passed through a normal pregnancy, and her child is now over five years of age and healthy. Three series of exposures of the spleen to radium had been made during the pregnancy. The woman died a year after the childbirth. Meurer[3] records a case of myelogenous leukemia in a 7-para who gave birth to living twins after a pregnancy of thirty-four weeks. While the blood from the maternal part of the placenta presented all the appearances of leukemic blood the children's blood was quite normal. The patient was delivered on February 20, and on March 15 roentgen-ray applications to the spleen were commenced and continued to the following June with marked improvement.

The use of benzol is fairly generally condemned. However, Stiènon[4] reports a case of myelocytic leukemia successfully treated with benzol after arsenic and the roentgen ray for six months had failed. Schisler and Brown[5] made a comparative study of the separate and combined action of benzol and the roentgen ray in rather a severe case of myelo-

[1] Quoted in the Lancet, 1921, **200**, 606.
[2] Bulletins de la Société Médicale des Hôpitaux, Paris, 1920, **44**, 1511.
[3] Nederl. Tijdschr. v. Geneesk., September 17, 1921.
[4] Le Scalpel, January 15, 1921.
[5] Medical Record, 1921, **99**, 505.

cytic leukemia. The roentgen rays and benzol together produced a rapid permanent fall in the white count, while the roentgen rays alone produced an immediate rapid fall, with a subsequent rise in the first instance to the same count as before exposure and in the second trial a decrease with subsequent rise to about one-third the count preceding exposure. The red count and hemoglobin were not markedly affected by either benzol or roentgen ray but increased steadily as the patient's condition improved. The differential count showed a more or less continuous relative increase of polymorphonuclear leukocytes with a corresponding fall of myelocytes. The relative lymphocyte count after a slight initial increase remained more or less stationary. The roentgen rays seemed to destroy polymorphonuclear leukocytes or to slow up their production, but relatively had no such effect on the red cells or their production. After roentgen-ray exposures the blood smears showed numerous disintegrating white cells. After the roentgen rays, the myelocytes were still persistent in the blood picture and in the various neutrophilic, basophilic and eosinophilic forms, the eosinophilic persisting longer than the basophilic. The roentgen rays in every trial produced a decrease in the absolute number of small lymphocytes but had no constant effect on the relative count. Myelocytes are relatively decreased by the roentgen ray with no constant effect on the absolute. Benzol, on the other hand, caused a steady fall in the absolute count but did not effect the relative myelocytic count.

Glandular Fever was described as long ago as 1889 by Pfeiffer. Although the disease is rare, Tidy and Morley[1] believe that a considerable number of cases are occurring at the present time. Reference was made on a previous page of this review to reports of this disease under new names, such as "acute benign lymphoblastosis" and "infectious mononucleosis." There are also certain clinical characteristics which together with the blood examinations might confuse the diagnosis with that of acute leukemia.

Tidy and Morley[2] and Morse[3] discuss the clinical manifestations and diagnosis. Morse's description is brief and to the point. The affection is supposed to have an incubation period of from five to ten days. The onset is sudden, usually with sore-throat and a feeling of stiffness in the neck, and often with upper abdominal pain or discomfort in the left hypochrondrium. Nausea and vomiting are common at the onset. The temperature is often normal in the morning and is seldom above 102° F. in the afternoon. Within a week the temperature has usually returned to normal. Physical examination reveals the swollen lymph nodes as the outstanding feature. Usually, the cervical chain is most involved, but the supraclavicular and infraclavicular, axillary and inguinal nodes are almost always palpable. In the first case here reported, the epitrochlears were also enlarged. The spleen is enlarged and tender in about 60 per cent of the cases. Aside from the lymph node enlargement, the blood count is most characteristic and tends

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[1] British Medical Journal, March, 1921, 452.
[2] Ibid., **1**, 452.
[3] Journal of the American Medical Association, 1921, **77**, 1403.

often to confuse the disease with acute leukemia. A rise in the white cell count to 17,000 or 20,000 is the rule. The stained smear reveals that the increase is due entirely to mononuclear cells. These cells are of the lymphoblastic type and there are many with bilobed Riedel nuclei. The average lymphocyte percentage runs from 75 to 85. The lymph nodes and spleen decrease in size more slowly, but the spleen is not usually palpable after the fourteenth day. The blood count gradually returns to normal, but this may take several weeks. The prognosis is favorable. Morley and Tidy state that only four fatal cases are recorded. The convalescence is noticeably slow, and a feeling of weakness persists for some time. In the first case here reported, the hemoglobin was 60 per cent during the illness, and about three weeks later reached only 75 per cent. The patient complained of considerable lassitude at this time. The anemia and the persistence, for some time, of palpable glands have been repeatedly observed.

In the differential diagnosis, Morse states that there are several conditions, such as tuberculosis, mumps and acute cervical adenitis, which glandular fever may simulate, but there is no trouble in differentiating them if a careful physical examination and a blood count are made. Acute lymphatic leukemia is ruled out with greater difficulty; but, usually, the milder course and the lack of hemorrhages in glandular fever, along with a study of the blood picture, are sufficient to rule out leukemia. The blood smear is quite different in appearance from that of leukemia. There is a lack of immature, atypical and degenerating forms of leukocytes, and the presence of large numbers of the bilobed or Riedel type of white cell is quite distinctive. In view of the favorable outcome of glandular fever, and the hopeless prognosis of lymphatic leukemia, a correct diagnosis is especially important.

Multiple Myeloma must still be classed among the rare diseases. Oftedal[1] reports a case with necropsy studies, and refers to Wallgren's collection of 118 cases up to 1920. Oftedal's case was diagnosed during life. In Branham and Lewis's[2] patient the symptoms simulated brain tumor with pronounced unilateral exophthalmos. The true nature of the case remained unrecognized until the necropsy. The patient was a victim of dementia and upon several occasions had been subject to severe trauma. Upon several other occasions, swelling of the face occurred. During one attack, a tooth was extracted, and, in another, erysipelas was diagnosed. Three months prior to death the patient complained of pain in his right leg. Examination showed enlargement of the right hip, with no evidence of a tumor growth. A moderate degree of tenderness was present. Three weeks later exophthalmos of the left eyeball was noticed. Although there were no signs of general intracranial pressure, a brain tumor was suspected. Impairment of vision was noted early. A well-defined, immovable tumor, the size of a hen's egg, over the region of the right trochanter, was present by this time. The patient died December 22, 1919. Tumor growths were found in the lumbar lymph glands, the neck

[1] Journal of the American Medical Association, 1921, **77**, 1547.
[2] Medical Record, 1921, **99**, 169.

of the femur, left parietal bone and right ilium.   Both Oftedal and Branham and Lewis call attention to the element of trauma in the etiology.

Wells[1] reports a case in which interesting pathologic studies were made. Although the condition was one of multiple myelomatosis of the bones, yet some features seemed to correspond perfectly to what has frequently been described as either angiosarcoma or multiple endothelioma of bone.   He states that a growth that begins as a myeloma may take on the characteristics of a neoplasm of vascular origin, with no remnants of the original tumor to be found in the entire bone tumor.   The space of this review does not permit detailed comment on Wells' interesting paper except to state that his observations lend support to the opinion expressed by others, notably Ewing, that many of the tumors described as multiple vascular endotheliomas of bone, and sometimes also as bone aneurysm, are really myelomas.   This view is in harmony with the fact that myelomas are the chief form of multiple bone tumors, and that the frequency, if not the existence, of true endothelioma, is becoming less and less supported.   It is, of course, probable that other bone tumors than myelomas may undergo the same sort of hemorrhagic necrosis and replacement by vascular new tissue.

BENCE-JONES PROTEINURIA occurs in 80 per cent of cases of multiple myeloma, according to Walters,[2] who reports 3 cases.   He states that the other diseases in which Bence-Jones proteinuria have been found are lymphatic leukemia, myeloid leukemia, myxedema, exophthalmic goiter, carcinomatosis, nephritis, hypertension and experimental poisoning by pyrodin.   Of Walter's cases, 1 had generalized carcinomatosis, 1 multiple myeloma, and in 1 the diagnosis was obscure. The most characteristic reactions of Bence-Jones protein are its precipitation from acid urine at temperatures of from $55°$ to $60°$ C., its disappearance at the boiling point with the formation of a clear solution and its reappearance as the solution cools.   Walter's conclusions in part are as follows:

1. A large quantity of albumin in otherwise negative urine in a patient with normal renal function and normal blood-pressure and a marked secondary anemia should suggest the possibility of Bence-Jones proteinuria, especially when bone lesions are present.

2. Bence-Jones proteinuria is significant from a diagnostic and from a prognostic standpoint of multiple myeloma, since it occurs in 80 per cent of all cases and usually is followed by death within two years.

3. The quantity of Bence-Jones protein excreted is independent of the protein intake, and during the night, when food is not taken, is only slightly less than the amount excreted during the day.

Blood Platelets. The increasing difficulty in obtaining brilliant cresyl blue led Buckman and Hallisey[3] to search for another dye that might be used for the vital staining of blood.   They found crystal violet (pentamethyl pararosanilin hydrochlorid) an easily procurable and most

[1] Archives of Surgery, 1921, **2**, 435.
[2] Journal of the American Medical Association, 1921, **76**, 641.
[3] Ibid., 427.

satisfactory vital stain for platelets. The technic which they have perfected allows of a simultaneous determination of platelets, red cells and white cells, which closely parallel those obtained by other and standard methods. The procedure which they describe is as follows: Blood is obtained from a vein and allowed to flow into a minature transfusion tube, evenly paraffined, attached to a paraffined hypodermic needle of 18 gauge. The tube that is used is similar to the one described by Lee and Vincent, and has a capacity of about 6 cc. As the blood wells up in the tube, the tip of a "red count pipette" is introduced and blood drawn up to the 0.5 mark. The pipette is then immediately filled with the diluting fluid to the 101 mark and shaken for three minutes. A drop from this pipette is then mounted in a Türck counting chamber in the usual manner. At the end of three minutes a red count may be made. At the end of five minutes a white count may be made, counting nine square millimeters of the field and using the high dry objective. When the specimen has stood for twenty minutes, all the platelets will have "settled" and a platelet count may then be made, using again the high dry objective and counting four square millimeters of the field. A second, and if need be, a third drop is similarly counted and the average of the counts taken. Red, white, and platelet counts may be made as long as four hours after the taking of the specimen.

The Diluting Fluid. Six gm. of glucose and 0.4 gm. of sodium citrate are dissolved in 100 cc of distilled water, and the solution is filtered. To this are then added about 0.02 gm. of toluene red, dimethyldiamidotoluphenazin, sometimes also called "neutral red." Solution is slow but ultimately clear. To this is then added 0.1 gm. of crystal violet, and the solution is gently heated to 60 C. and held at that temperature for five minutes. It is allowed to cool slowly to room temperature and centrifuged for ten minutes at 2000 revolutions a minute. The supernatant liquid is then filtered twice, each time through three thicknesses of No. 30 Whatman filter paper (dry). The solution is preserved by adding 0.2 cc of formaldehyde solution and then keeps indefinitely.

Blood Transfusion. Blood transfusion has become a widely practised procedure. In properly selected cases, it is followed by brilliant results. The indications for its use are: (1) In loss of blood, both of the acute type and that which results from long-continued small bleedings; (2) in disorders of the blood when it is desired to stimulate the hematopoietic organs, to increase coagulability, to increase the oxygen carrying capacity, to improve the general nutrition; (3) in shock, especially if associated with hemorrhage. In the selection of the donor the laboratory must make three tests: (1) Wassermann, (2) ordinary and differential count and (3) typing for group classification.

Ravdin and Glenn[1] report the results of 186 transfusions in 87 patients. Their conclusions are as follows: Transfusion is a specific in acute hemorrhage where the "limit of bleeding" has not been reached; in melena and in the hemorrhage of hemophilia. It is of definite value

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[1] American Journal of the Medical Sciences, 1921, **161**, 705.

in primary pernicious anemia in hastening and prolonging remissions. It is indicated in cases of severe secondary anemia. After transfusion, operations on debilitated or anemic individuals may often be safely undertaken that otherwise would involve serious risk. Transfusion in shock is not as efficacious as in cases of shock associated with hemorrhage. The writers have not been able to prove the value of transfusion in acute infections, but in chronic infections they have had results justifying its use. Transfusion is of unproved value in acute leukemia. In aplastic anemia, it is at the most a temporizing procedure. The difference, as far as reactions are concerned, between the citrate method and the Kimpton-Brown method they have found to be practically *nil* and the simplicity of the former warrants its preference.

The deleterious effect of sodium citrate employed in blood transfusion is discussed by Unger,[1] who states that even in low percentages the red blood cells are rendered more fragile. The value of citrated blood to a patient suffering from hemolytic disease is considerably lessened by reason of this influence. The biologic tests demonstrate that the transfusion of unmodified blood is of far greater value than blood modified by the addition of sodium citrate. Sodium citrate diminishes the available quantity of complement in two ways: by its direct action on complement itself, and by introducing into plasma an anti-complementary substance which inactivates complement. This substance is derived directly from the bodies of red blood cells. Sodium citrate also reduces almost to *nil* the function of opsonins, and practically destroys the phagocytic power of white blood cells. Furthermore, the phagocytic index of the blood of various donors differs. Since complement and the phagocytic power are of prime importance in the protective action against pathogenic organisms, unmodified blood from a donor with high phagocytic index should be employed when attempting to combat local or general infections by means of transfusion. In selecting a donor, attention should be paid to the finer qualitative differences in the blood.

The transfusion of whole blood requires a higher degree of skill than does the giving of citrated blood. This method of transfusion is available only when a surgeon can be obtained. The transfusion of citrated blood, however, is a simple procedure, which requires but little practice to render simple and safe. Hoffman and Habein[2] describe a simple apparatus available to the physician who performs only an occasional citrated blood transfusion. There are some cases, however, in which citrated blood is unsuited. Bernheim[3] mentions two types of case: (1) That in which there has been a hemorrhage of such intensity that the extreme limits of bleeding have been reached, and the patient is in such a state of shock that everything in the nature of additional shock must at all hazards be avoided. (2) Those states of anemia, either primary or secondary, in which the blood depletion has progressed to such limits that the patient is almost dead. Bernheim further states that we may

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[1] Journal of the American Medical Association, 1921, **77**, 2107.
[2] Ibid., **76**, 358.   [3] Ibid., **77**, 275.

expect reactions of greater or less severity in from 20 to 40 per cent of all citrate transfusions. It is highly desirable, therefore, to use whole blood transfusions in which the percentage of reactions is hardly 5 per cent in those cases in which the occurrence of a reaction might be fatal.

The occurrence of hemoglobinuria after a second citrated blood transfusion with the same donor is reported by Thalhimer.[1] The patient was a boy transfused with his father's blood. A direct test of these bloods, made both by macroscopic and by microscopic methods, detected no agglutinins. The transfusion was performed by the citrate method and was followed by only a mild febrile reaction. Eighteen days later a similar transfusion was performed with the same donor, and after about 150 cc had been given, a most severe and unexpected reaction occurred. The transfusion was, of course, immediately stopped, and a few hours later the patient voided very dark, hemoglobinuric urine. This showed that hemolysis had occurred, and explained the reaction. Thalhimer points out that the two errors were: (1) performing only direct tests on the two bloods and not also determining the blood groups; (2) not repeating the direct tests before the second transfusion. Neither the blood group method nor the direct test alone, is sufficient to safeguard against the danger of agglutination or hemolysis occurring after a transfusion. This is especially true in transfusing children, whose agglutinins are more likely to be weak than is the case with adults. The two types of tests, if they serve no other purpose, serve as a check on each other. If the same donor is used for more than one transfusion on the same individual, the direct tests must be made each time before each transfusion. This is necessary because agglutinins and hemolysins originally absent may develop against a donor's blood when the donor is used more than once in the transfusion of the same patient.

Blood transfusion is an absolute remedy for cases of *hemorrhagic disease of the newborn*, according to a number of observers. Robertson,[2] in the Hospital for Sick Children, Toronto, uses the syringe cannula method by preference in these patients. The freshly introduced blood not only stops bleeding, but replaces the lost blood. He considers the cure of the hemorrhagic condition to be accomplished practically at the end of the transfusion. The amount to be given varies with the weight of the infant, but a good working rule is not to exceed 15 c.cm. per pound of body weight. The transfusion is completed usually in ten to twelve minutes, the actual time of injection being about three to four minutes for 100 c.cm. of blood. Following transfusion, if the bleeding has been from the bowel, old dark blood is passed during the first twenty-four hours. The necessity of obtaining a compatible donor is not as great as in the case of older children or adults, as in many of the infants agglutinins are not established at birth, or if so, are apparently weak. When the father is the only donor available, Robertson has used him without preliminary grouping tests. If circumstances permit of it, it is safer to have a compatible donor or a universal donor

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[1] Journal of the American Medical Association, 1921, **76**, 1345.
[2] British Medical Journal, 1921, **1**, 791.

(Group IV, Moss grouping). Robertson states that in a series of 40 cases of hemorrhagic disease of the newly born transfused at this hospital and elsewhere, 4 died, 2 of these from associated sepsis of the umbilical cord and 1 from intracranial hemorrhage, which was extensive before transfusion. The fourth case was moribund when admitted to the hospital. Jervell[1] and Laurie[2] report instances of melena neonatorum in which prompt benefit followed blood transfusion.

The transfusion for malnutrition in infants may be accomplished by the use of the superior longitudinal sinus as practised by Burk and Fischer.[3] These observers performed 14 transfusions on infants ranging in age from nine days to six months, using one ounce of a 0.3 citrated blood. The injection was without harmful effect and was followed by marked improvement in 4, slight improvement in 6, and no change in 2. Feeding should be delayed for at least an hour after transfusion, otherwise vomiting may occur. The treatment is of value in cases of malnutrition, hemorrhagic disease, and cachexias following acute infections, and it improves the general condition of infants with gastro-intestinal disorders, especially in cases suffering marked dehydration after failures of hypodermoclysis, rectal instillations, and venous infusions. The prognosis is improved in premature infants after transfusion.

Robertson, Brown and Simpson[4] have found that some of the blood groups are definitely established at birth, and, although the agglutinins may not be established until later, an effort should be made to determine the blood compatibilities when transfusion is contemplated. In 56 per cent of the male parents and 57 per cent of the female parents which they studied, the blood group was the same as the child; in 25 per cent both mother and father were in the same group as the child. These observers have had a large experience and consider the syringe cannula method with the use of whole blood as preferable to the citrate method.

Gemmell[5] emphasized the need for blood compatibility study when the transfusion of the maternal blood into an infant was contemplated. If they differ, and Gemmell states they do in one-third of all cases, another donor should be selected.

The practice of using the patient's own blood in transfusion in extra-uterine pregnancy has been practised with success by Klopp,[6] of Philadelphia. Schweitzer[7] has also used the patient's own blood in the transfusion of 21 patients among 34 patients which he operated upon for ruptured ectopic pregnancy with hemorrhage. He considers the method a useful life-saving procedure. One patient developed a fatal hemoglobinuria.

The use of blood transfusion in nitrobenzol poisoning when symptoms are severe is advocated by Hindse-Nielsen.[8] He reports a case in which

[1] Norsk Magazin for Laegevidenskaben, 1921, **82**, 778.
[2] British Medical Journal, 1921, **1**, 527.   [3] Medical Record, 1921, **100**, 751.
[4] Northwest Medicine, 1921, **20**, 233.
[5] British Medical Journal, 1921, **1**, 641.   [6] Personal communication.
[7] Münchener Medizinische Wochenschrift, 1921, **68**, 699.
[8] Ugeskrift for Laeger, September 9, 1920.

a critical condition continued until the transfusion was performed, when prompt recovery followed.

Ashby[1] made a study of the length of life of the normal blood-corpuscles and the mechanism of their removal from the circulation by the study of the elimination of transfused blood from a group unlike that of the recipient. He has shown that the length of time that transfused blood remains in the circulation varies greatly and that the elimination is not a continuous process, but takes place in more or less cyclic crises, so that the responsibility for the disappearance of transfused blood from the circulation seems to rest more heavily on this cyclic activity of the body than upon the condition of the corpuscle. Group IV transfused blood in a recipient of an unlike group is eliminated by a blood-destroying activity of the body. This blood-destroying activity is periodic, both in men and women, and in women coincident with menstruation. It is not known whether this blood is eliminated, as part of a general blood-eliminating effort, as a foreign body. In pernicious anemia patients, Group IV transfused blood has remained in the circulation with destruction of the patient's own blood, and with destruction of transfused blood of the patient's group. · If the elimination of Group IV blood results from a normal blood-eliminating process, a certain pressure of elimination must be attained before the threshold is reached for the elimination of Group IV, which is apparently more difficult to destroy. The elimination of the transfused blood probably takes place as part of a period of blood-destroying and blood-producing activity of the body, although direct evidence to this effect is so far lacking.

An attempt was made to obtain some understanding of the mechanism by which blood destruction is brought about, by means of the study of the elimination of Group IV transfused blood. Thirty-three patients with pernicious anemia not of Group IV were given Group IV transfusions. This study seems to indicate that although in some cases at certain times there is much blood elimination, on the whole, blood destruction is quiescent. The factor of production is an unknown quantity. Group IV transfused corpuscles are usually not eliminated so quickly as they are in transfused persons without blood disease, so that so far as Group IV corpuscles are concerned there is no abnormal blood elimination. Since these corpuscles are not eliminated the activity of any corpuscle poison during these periods is ruled out. Evidence is presented to show that there is no hemolytic toxin producing the anemia in pernicious anemia. Partial evidence is presented to show that the periods of active blood destruction which are seen as the exception in pernicious anemia cases during a series of transfusions are due to the activity of the blood-destroying organs of the body rather than to the intrinsic weakness of the pernicious anemia blood corpuscle. It is questionable whether blood destruction is as important a factor in producing the anemia of pernicious anemia as it is at present usually assumed to be.

[1] Journal Experimental Medicine, 1921, **34,** 127, Ibid.; 147, abstract International Medical and Surgical Survey, 1921, **2,** 892 and 893.

Hodgkin's Disease. A diagnosis of Hodgkin's disease cannot be considered conclusive without the examination of tissue and a microscopic picture in agreement with the clinical description. This is the opinion of Lemon and Doyle[1] who report clinical observations on Hodgkin's disease with special reference to mediastinal involvement. Twenty-three of the 26 patients whose records form the basis of their report submitted to the removal of glands which were microscopically found to be affected with Hodgkin's disease. Seventeen of the patients were males and 9 were females; the average of the former was thirty-five and four-tenths years, and of the latter thirty-three and eight-tenths years. Because of the ancient controversy with regard to the importance of tuberculosis as an etiologic factor in Hodgkin's disease, an inquiry was made into the family history of the patients. One patient reported that a cousin had tuberculous glands in the neck and another patient believed that a maternal aunt had died from pulmonary tuberculosis. Roentgen-ray examination revealed evidence of tuberculosis in only 1 patient and this could not be confirmed by clinical or microscopic methods. Lemon and Doyle state that it seems extremely unlikely that recent throat infections are of importance in the etiology of the disease. In only 1 instance was a definite disease condition found in the tonsil. They believe that the occurrence of the condition in the cervical glands has not been accounted for. Reed did not find the report of an authentic case in which the condition had not started in the cervical glands. In Lemon and Doyle's series of cases the cervical glands were involved in 100 per cent, but the latter were not always the first to be affected. It is quite probable that other glands may be primarily involved.

The symptoms in most instances were typical of cases in which there was no mediastinal involvement. Many of the patients complained of weakness, anemia, loss of weight, nightsweats, diarrhea and anasarca, but such symptoms could be construed as common to all the patients. In discussing the chest symptoms, Lemon and Doyle note that dyspnea, severe enough to be offered as a complaint, was present in 6 instances. Orthopnea was complained of in 2 cases. Dysphagia due to esophageal pressure occurred in 1 case. Dilated veins over the chest were present in 3 cases and over the abdomen and the chest in 1. Cyanosis and swelling of the face and the neck was, of course, present in these 3 cases, and could be easily demonstrated by inverting the patient for a short time. Tachycardia and palpitation was complained of in 2 cases and dizziness in only 1. Cough was sufficiently urgent to be a complaint in 4 cases, and in 2 the sputum was excessive. Fluid was found in the chest, in one thoracic cavity or in both, in 8 cases, an incidence of 30.7 per cent. This can be explained by the masses of glands exerting pressure on the pulmonary veins and on the azygos. It is significant that the recurrent laryngeal, vagus, and sympathetic nerves, and the thoracic duct escaped direct pressure and thus did not provide signs of help in making a diagnosis, also that few of the patients made com-

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[1] American Journal of the Medical Sciences, 1921,|**162**, 516.

plaints directing attention to the chest, although in 1 the right thoracic cavity was found to be filled with fluid. Chyloid fluid was not observed.

In the physical examination of the chest Lemon and Doyle found percussion unsatisfactory and d'Espine's sign of no help. In the diagnosis of thoracic glandular enlargement dyspnea with cough resembling whooping cough; dysphagia from esophageal pressure; vomiting from pressure on the vagus; and edema of the upper part of the abdomen and serous effusion into the thoracic cavity are to be emphasized. The finding of glandular enlargements in neck, axillary region, etc., is a diagnostic aid of first importance. Splenomegaly was discovered in 23 per cent of Lemon and Doyle's series of patients. Blood counts were made in 23 cases; no material changes from the normal were noted. In none of the cases were there indication of an increase in large mononuclear cells, as described by Bunting, nor of an excess of lymphocytes that is so general in late stages of the disease. The roentgenogram reveals a bilateral feathery shadow passing outward from each hilus. A pathologic diagnosis hardly should be expected from the roentgenographic findings, but in 8 cases a positive opinion was reached. In 4 cases the picture was complicated by the presence of fluid; in 4 the presence of glands was recognized but their character was undefined. In 3 a suspicious shadow or thickening was seen; in 1 the diagnosis was sarcoma; in 5 the shadow was reported as that of a mediastinal tumor; and in 2 no positive conclusions were reported. The roentgenogram must be considered a routine method of examination inasmuch as it is essential to know of mediastinal complications both from the standpoint of prognosis and of treatment.

Lymphosarcoma, Lymphatic Leukemia, [Leukosarcoma, Hodgkin's Disease. These clinically allied conditions have been much discussed both as to their relationships and their classification. Webster[1] has recently summarized a study of 123 cases of lymphosarcoma, lymphatic leukemia, leukosarcoma and Hodgkin's disease. He separates *Hodgkin's disease* or lymphadenoma as a distinct disorder, which can be definitely diagnosed by microscopical examination of a single gland, and an accurate prognosis thus provided. Twelve cases are reviewed, all of which presented general glandular enlargement with involvement of liver and spleen. Tuberculosis was present in 2 cases, and 3 cases showed invasive tumor masses associated with the mediastinal or cervical glands. Webster states that lymphoscarcoma, lymphatic leukemia and leukosarcoma are probably different manifestations of the same disease and suggests the term "lymphadenosis, leukemic or aleukemic" as expressive of this idea. He considers that the disease is not a neoplasm but a direct response on the part of the lymphocytes to a chemotactic influence exerted by the disease-causing agent. The presence of this substance in any tissue or organ produces there a local accumulation of lymphoid cells. When evidence of amœboid activity on the part of the lymphocytes occurs it is indicative of a rapid fatal course. Hodgkin's disease is a reticulo-endothelial cell proliferative process,

[1] Johns Hopkins Hospital Bulletin, 1920, **31**, 458 and Johns Hopkins Hospital Reports, 1921, **20**, 251.

rather than a lymphocytic proliferative process and may be diagnosed microscopically. Lymphosarcoma cannot always be diagnosed microscopically. Leukosarcoma, which also is an invasive tumor, shows blood changes of a leukemic character. One of the cases of leukosarcoma reported by Webster began as a localized tumor of the chest and developed a typical lymphatic leukemia after roentgen-ray treatment. It would seem from this case that leukosarcoma combines the features of lymphosarcoma and lymphatic leukemia, and that a localized lymphosarcoma may under certain conditions become generalized and with a blood picture of lymphatic leukemia may terminate as a leukosarcoma.

Very important in this connection is the mode of spread of the lymphosarcoma group which, regardless of its primary site, extends in a characteristic manner first by local infiltration and later by the blood stream to parenchymatous organs, lymph glands, bone marrow, etc. At this stage only the negative blood findings differentiate the case from leukosarcoma and only the blood and the presence of a local infiltrating mass differentiate it from lymphatic leukemia. Finally, in lymphatic leukemia one may see a similar mode of progression. The first cases, showing no increase in the number of blood lymphocytes, presented at autopsy hyperplastic lymphoid tissues with generalized infiltrations. Other cases, with a positive blood picture, showed more or less localized lymphoid involvement. The main group is quite typical but the last case developed, during the course of the leukemia, large infiltrating masses in the inguinal regions. It appears, then, that in the leukemia group some cases closely resemble certain types of lymphosarcoma, while others approach leukosarcoma. Microscopically, the lymphatic infiltrations of the organs in these diseases differ in quantity but not in quality. Distant lymph nodes appear the same in leukosarcoma as in lymphosarcoma and leukemia. The parenchymatous organs and even the bone marrows are indistinguishable. Although the size and shape of the cell varies in the several cases it still retains its lymphoid character.

It appears not unlikely, then, that leukosarcoma, lymphosarcoma and lymphatic leukemia are different manifestations of the same disease. In early life the primary focus may be in the small intestine or mediastinum. The disease then runs a rapid and fatal course spreading locally or generally (lymphosarcoma), occasionally to terminate with manifestations of lymphatic leukemia (leukosarcoma). Later in life the focus may be anywhere and the course is more protracted. Extension, however, occurs in a similar manner. In many ways the disease is quite comparable with tuberculosis, which in the young localizes in the chest or intestines, later to become spread more diffusely, and in adult life assumes many odd forms, attacking the kidney, uterus, skin, etc.

The relation of Hodgkin's disease to sarcoma with a report of 2 cases was the subject of a study by Mueller.[1] In 16 cases of Hodgkin's

[1] Journal Medical Research, 1921, **42**, 325; abstract International Medical and Surgical Survey, 1921, **2**, 1566.

disease, the diagnosis was confirmed microscopically in 14. In 2 cases the histologic studies showed a change in the structure from typical lymphogranuloma to round-cell sarcoma or *vice versa*. In 1 of these cases, the disease exhibited malignant neoplastic properties with invasion of the lungs, aortic wall, and spinal canal. The 2 cases illustrate the difficulty of determining the nature of the underlying process in Hodgkin's disease and its relation to sarcoma. They also raise the question: Is Hodgkin's a true neoplastic disease on the basis of a chronic toxic tissue irritation, or is it an infectious process possessing certain similarities to sarcoma, but no actual relation? Mueller concludes that from a histologic-anatomic point of view, the opinion seems justified that lymphogranuloma and round-cell sarcoma of the lymph nodes are only different expressions of the same process. The cause of the sarcomatous infiltrating course of the disease is to be sought in the individuality of the patient, in the amount and virulence of the causative agent, and the duration of its action on the lymphatic tissue.

OPHTHALMOLOGY.

By JOSEPH W. CHARLES, M.D.

Ophthalmia Neonatorum. Brubacher[1] states that the number of cases of ophthalmia neonatorum has materially increased since 1917, and that the gonococci seem to have acquired special resistance to silver, implying that they have also a specially great virulence, because the instillation of ordinary 1 per cent solution does not ward off the ophthalmia but merely retards its development until the sixth to the tenth day. However, one may also consider that midwives and medical men may not be quite so thorough in its application as obtained before the medical services were disintegrated by the war, and certainly the application of the 1 per cent solution to the turned lids is superior to the old Credè method of simply instilling a drop of the 2 per cent solution on the cornea.

Ophthalmia Neonatorum Before Birth. Dundas[2] reported the case of a new-born babe with red and edematous lids, and a purulent discharge from both eyes. Evidently, the case was one of intrauterine infection made possible by draining away of the liquor amnii, "and presumably the presentation had been a brow converted into an occipital during labor." After death on the tenth day, extreme intracranial congestion was found, the sinuses were full of fluid blood, with intense injection of the pia. A purulent exudate was also found on the middle of the base of the skull from the optic commissure backward. The eyeballs were intact.

The Credè Method of Prophylaxis in Careless Hands. Since Wiener, a number of years ago, reported a case of a hemophiliac baby, which bled to death after the use of the Credè method of prophylaxis against ophthalmia neonatorum, it has occurred to me that there might be some dangers attached to the unrestricted use of silver nitrate by unskilled persons, especially in view of our more recent laws governing midwives and physicians.

The *Budapesti Orvosi ujsag*, or Medical News[3] reports a case in which a 10 per cent solution of silver nitrate was dropped into the eyes of a new-born babe instead of the usual 1 per cent solution. Opening the eyes revealed a gelatinous mass, and total blindness resulted from perforation of the cornea and prolapse of the iris. Therefore, the

[1] Monatsschr. f. Geb. u. Gynäkologie, Abstract, Journal of the American Medical Association, May 28, 1921, p. 1541.

[2] London Lancet, January 15, 1921, p. 122; Abstract, Journal of the American Medical Association, February, 1921, p. 550.

[3] Abstract, Journal of the American Medical Association, September 3, 1921, p. 802.

highest board of sanitation intends to issue a new order prescribing instead a 1 per cent solution of silver acetate because the latter is not soluble in a higher percentage than 1 : 100.

Quite a propos then will be found the editorial of Jackson, concerning *Detail in Therapeutic Measures*[1] in which he remarks the inadequacy of the average teacher's instruction concerning, or perhaps the average pupil's lack of appreciation of, the smaller details of treatment of the eye, and an equally sensible editorial[2] warning against the overtreatment of the eye by too frequent application of remedies, and especially in ophthalmia neonatorum.

Trachoma. EXPERIMENTAL STUDIES ON TRACHOMA. Last year, Eaton expressed his opinion that the most potent factor in the transmission of trachoma is the interhuman contagion rather than a certain fly which he had formerly believed to be responsible.

Nicolle and Guénod[3] have found that the infective agent is a filtrable virus, passing through the Berkefeld V filter, is destroyed by heating to 50° C. for one-half hour, and that it may be preserved in glycerol at ice-box temperature for seven days. The chimpanzee, baboon and rabbit are susceptible, but the rat, cat and guinea-pig are not. The virus survived five transfers from rabbit to rabbit, and has been recovered from the eye of the rabbit one year after inoculation. It was preserved in the testicle of the rabbit for thirty-seven days. Their more recent work shows that recovery from one attack does not render the animal immune to a new infection. Because of these discoveries, they feel that there is some hope of finally treating trachoma by means of serums or vaccines.

In addition to isolation of patients, the rooms should be protected from flies, and there should be a systematic destruction of flies because the authors believe that the fly may transmit the disease for a period of twenty-four hours after contact.

THE DIAGNOSIS OF TRACHOMA GRANULES UPON THE CORNEAL LIMBUS. Hiwatari[4] believes that many of the diagnoses made of trachoma granules at the limbus are based on certain misconceptions of the normal and pathologic anatomy of that region. He calls attention to three points, which seem to have been overlooked.

1. Cicatricial contraction may move the fornix so that some of its granules advance to the region of the limbus and seem to have developed there.

2. During the course of trachoma, a combined infection from the Koch-Weeks bacillus or pneumococcus may cause "phlyctenules," or at any rate infiltrations which are not true trachoma granules.

3. The diagnosis of true trachoma must depend upon a microscopic examination. The subepithelial layer of the limbus shows a network of small ledges resembling papillæ in the sections, and this is the part of the limbus which is most adherent to the subjacent tissue. The genuine

[1] American Journal of Ophthalmology, May, 1921, p. 350.
[2] Ibid., October, 1921, p. 781.
[3] Archiv. d. Instit. Pasteur de l'Afrique du Nord, July, 1921, Abstract, Journal of the American Medical Association, September 17, 1921, p. 943.
[4] American Journal of Ophthalmology, March, 1921, p. 200.

trachoma granule on the limbus develops exactly in that part or closely in its neighborhood, and must have the following structure: "The marginal portions of the granules, which represent usually a narrow zone, must consist of the small lymphocytes partly emigrating in the epithelial layer; while the wider interior parts, the germ center in my opinion, must consist of large lymphoid cells."

THE TREATMENT OF TRACHOMA. Birnbaum[1] reports his success in the treatment of trachoma during the war with the usual well-known remedies, but stresses the importance of daily treatment by the physician, and especially of massage.

In the large granular type, he uses Knapp's forceps for expressing, following this by rubbing the conjunctiva with cotton soaked in 1 to 1000 sublimate solution.

Following this, active massage of the conjunctiva is systematically practised, using counterpressure on the skin of the lid. A glass rod, bent at one extremity, is very useful in massaging, counterpressure being made with the finger. At intervals, copper sulphate crystal is applied more or less strongly, according to the amount of cauterization required. This treatment should render the aspect of the conjunctiva more or less normal in four to six weeks; alum is then used, followed later with a solution of zinc sulphate.

The papillary form is less amenable to treatment and requires twice as long a time. The author uses a 2 per cent silver nitrate solution until the humid condition has disappeared. This is followed with the copper treatment and massage. Twice a week a 1 to 400 sublimate solution is rubbed into the conjunctiva, which produces a very lively reaction. Four to five months ought to suffice for the most refractory cases.

He does not consider corneal complications as contraindicating the use of the silver nitrate and copper; and he has never had to employ any of the radical operations, such as excision of the cul-de-sac, incision of the tarsus or electrolysis.

Molluscum Conjunctivitis. Harold and Sanford R. Gifford[2] call attention to the fact that one or two nodules of molluscum contagiosum on, or near, the lid border can cause an intractable form of chronic conjunctivitis. These nodules present a pearly-white, waxy appearance, vary in size, and are usually easy to differentiate from milia, warts and fibromata by their central depression from which a cheesy material can often be expressed. They have seen about a dozen such cases in the last fifteen years and in more than three-fourths of the cases only a single nodule was present. A whole nodule was transplanted from the cheek to the skin of one of the Giffords with negative results.

Herpes of the Cornea after Antityphoid Vaccination. Henri Le Roux[3] reports 2 cases of herpes of the cornea, which appeared two days and three days, respectively, after antityphoid vaccination.

One eye only was affected in each patient, and the author states that there has been no case reported having both eyes attacked.

[1] Arch. d'Oph., May, 1921, p. 298.
[2] Archives of Ophthalmology, May, 1921, p. 227.
[3] Arch. d'Oph., February, 1921, p. 112.

Both patients entered the hospital with vision of the eye affected $\frac{2}{10}$. The first case was discharged cured in four weeks, with normal vision. The second case was treated also for four weeks; vision at time of discharge not given.

Mention is made of 2 cases reported by Morax, and of 3 cases reported by Gloagen. Both of Morax's cases had the vision considerably reduced by resultant scars.

In the author's opinion, herpes probably follows antityphoid vaccination quite frequently, but, when it is on the buccal or nasal mucous membrane, it may pass unnoticed. On the conjunctiva, and especially the cornea, it is much more serious, and the importance of early diagnosis and treatment should be recognized.

Aubineau[1] states that ocular complications following antityphoid vaccination are represented by a sudden herpetic keratitis.

He has found 11 cases in the French literature. A lively general reaction had always been noted following the first injection in these cases and appearing in from one-half to twelve hours after the vaccination. The abrupt monolateral corneal eruption, preceded or accompanied by naso-labial herpes, was noted from twelve to forty-eight hours after the general reaction. The keratitis necessitated treatment from fifteen to sixty days, and in the majority of cases caused permanent diminution in vision.

FURTHER OBSERVATIONS ON THE VIRUS OF HERPES FEBRILIS. Further observations on the virus of herpes febrilis are reported by Kovy.[2] He summarizes his findings as follows:

1. In 25 inoculations with herpetic material from different sources upon rabbits' cornea there occurred 22 times a polymorphous microorganism in the culture, which must be classified among the mycobacteria.

2. They succeeded 3 times in growing a culture direct from a herpes labialis.

3. In generally sick animals, the microörganism could be isolated 3 times from the blood, and from the spleen. At the same time, the spleen-pulp yields positive inoculation.

4. There occurred for the most part in the cultures several forms together; one saw also isolated a pure culture of a pure form. These could be developed into other forms through culturing.

5. In a sterile preparation from the conjunctival secretion and the corneal infiltration, the different forms could be found.

6. The microörganism grows well at 37° and also at room temperature, better aërobe than anaërobe.

7. The same is overwhelmingly Gram-negative.

8. The culture of the microörganism, whether there was a mixture of different forms or a pure culture of one form, could be carried from rabbit cornea to rabbit cornea as easily as the original material.

9. The virulence remained present a long time. One was able to obtain results with a culture, which was isolated from the eye ten weeks before.

Many microphotographs of these organisms are shown.

[1] Arch. d'Oph., December, 1921, p. 741.
[2] Klin. Monat. f. Augenheilk., 1921, p. 75.

Bilateral Symmetric Corneal Abscess Coincident with Pneumonia. A. Bichon[1] reports a case of bilateral symmetric corneal abscess, which developed in a male, aged thirty-nine years, during the course of a pneumonia. The right eye began to have blurred vision on the third day after the incidence of the disease, and three days later the left eye suddenly became violently painful. When seen by the author a month later, both corneæ had an abscess in the inferior nasal quadrant. Bacteriologic examination showed pneumococci associated with staphylococci and Weeks bacilli. The left eye was lost from panophthalmitis; the right recovered with vision $\frac{3}{10}$.

Since it is well known that endogenous infection may develop in the course of, or following, infectious diseases, such as variola, roseola, typhoid, pneumonia or pyemia, and since in this case there had been no conjunctivitis or traumatism, the author reports it as a metastatic infection of both ocular globes.

A Case of Acute Parenchymatous Keratitis in Parotitis Epidemica. Geis[2] describes a case of a girl of ten years who was the third of four children in the family to contract mumps. Swelling occurred in the left parotid only, with a temperature of 103° F. After five days the swelling had subsided, and the patient left her bed. The same day the left eye became red, and on the following morning the mother noted a gray clouding of the left eye.

This clouding, examined by the specialist, proved to be a thick, gray diffuse opacity, most marked in the center. Examined with the binocular loupe there could be seen gray streaks crossing each other, in part running in a radial direction in the deeper layers. Marked pericorneal and ciliary injection; vision was hand movements in the left eye. No change in these gray streaks or the occurrence of spaces could be observed with the loupe.

Seven days after the beginning of the eye trouble, the left eye was entirely free of irritation and the cornea was entirely clear.

The author thinks the corneal involvement here was due to the toxic action of the exciting cause of the mumps leading to an extravasation of the fluid into the corneal parenchyma.

The Influence of Ocular Tension upon Corneal Diffusion, with Certain Clinical Facts. Colombo,[3] having in mind the prompt amelioration in serpiginous ulcer following the voluntary perforation of the cornea, but disclaiming any intention of seeking to prove whether there exist any true spaces in the corneal parenchyma, or whether such spaces may exist potentially in pathologic conditions, has recently carried out some experiments which show that the filtration through corneal tissue is much more prompt in eyes where the normal intra-ocular tension has been lowered.

The experiment was made on the eyes of adult rabbits. A disk was removed by trephining the center of both eyes of the animal, the instrument stopping short of perforation, and an emulsion of fluorescein was instilled into each eye and thoroughly washed out in a half minute.

[1] Arch. d'Oph., February, 1921, p. 116.
[2] Klin. Monatsblätt f. Augenheilk., 1921, p. 67.
[3] Annales d'Ocul., May, 1921, p. 368.

Paracentesis was done at the limbus of one eye, the wound being reopened at intervals of five minutes to keep the aqueous well drained off.

It was found that in the eye on which paracentesis had been practised the coloring matter was diffused through the cornea much more rapidly than in the other eye, this facility of filtration evidently being due to the absence of compression, which the cornea undergoes by reason of the intra-ocular tension.

The author thinks this experiment might indicate the possibility of doing frequently repeated paracentesis at the limbus in hypopyon keratitis if precaution were taken against intra-ocular infection, which I believe would be rather difficult of accomplishment yet the relief of tension has seemed to accomplish wonders in some cases and if it is not accomplished many of these cases are already lost from *infection of the globe* after all.

A Contribution to the Pathogenesis of Keratitis Parenchymatosa and the Basis of the Neuropathic Constitution. Kranpa,[1] from his observations in many cases of congenital syphilis, concludes that the descendants of congenital leutic individuals are sensitive to a high degree to a new luetic infection and equally so whether this occurs *in utero* or in later life. He thinks the cornea and the nervous system offer little resistance to a reinfection with the spirochetes. One is compelled to concede a neuropathic constitution to cases of this kind, and they are said to belong to the typus cerebralis. The belief is false that congenital lues produces only inferior individuals.

Human Myiasis. Wright and Patton[2] reported in the *Indian Medical Gazette*, February, 1921, the case of a Hindu woman aged thirty years, whose "supraorbital and interorbital regions were alive with maggots; the bones had been extensively attacked; the surrounding sinuses were freely involved; the dura was not exposed. The eyeballs were exposed, proptosed, and pushed outward." One cornea was ulcerated. Marked edema and foul discharge were present. Permanganate and turpentine were used, and 50 maggots were removed the first day and 30 the next. Chlorine solution and iodoform packing were then used. The extrinsic muscles had been extensively destroyed. Prognosis was good for life, but poor for sight. The maggots are the mature larvæ of Chrysomyia bezziana Villeneuve, which deposits its eggs only in the diseased tissues of man and animals. Therefore the eggs were laid directly on an ulcerated surface in this case the result of the lancing of an abscess on the eyebrow and not within the nose. However, they may result from the attraction, by a nasal discharge, of the female to the inside of the nostrils.

Metastatic Episcleritis Furunculiformis. Kramer,[3] in an article entitled Metastatica Episcleritis Furunculiformis, reports a case of this condition from his own practice and briefly reviews all cases of a similar nature found in the literature.

[1] Klin. Monatsblätt f. Augenheilk, 1921, p. 218.
[2] British Journal of Ophthalmology, July, 1921.
[3] Klin. Monatsblätt f. Augenheilk., 1921, p. 411.

A young man, aged twenty-two years, after suffering for three months with innumerable furuncles, developed what was at first called scleritis of the right eye. Under hot applications there finally formed a small swelling the size of a pea upon the lateral half of the eye at the corneal margin. This prominence was well outlined, shelved away abruptly so that it projected in a hemispherical form; it was covered by smooth conjunctiva, distinctly fluctuated, and was very painful. The growth was split by a broad horizontal incision, which emptied out only a little crumbly pus. Through culturing, this secretion was found to contain staphylococcus pyogenes aureus. The further course closely followed that of a typical skin furuncle. Several days after incising, a pus plug or core was thrust out whereupon rapid healing occurred. During the entire course of the inflammation there was no involvement of the iris or deeper structures.

The author reports finding in the literature 15 other pure cases of metastatic episcleral formation of a furuncle. In 10 (62.5 per cent) of these, which was all that were bacteriologically examined, the Staphylococcus pyogenes aureus was found to be the cause. Involvement of the iris varied between the slightest irritation to the severest iritis. Prognosis is good.

Glass-workers' Cataract. The Glass-workers' Cataract Committee of the Royal Society[1] has analyzed with the spectroscope the radiations emitted from molten glass, and has reached the following conclusions: That no x-rays are emitted, but that luminous and ultra-violet rays are thrown off in considerable amount; that the PREPONDERANT EMISSION WAS OF HEAT RAYS, also that the luminous rays were not the source of the cataract nor the ultra-violet radiation insofar as any direct action upon the lens was concerned, but that the evidence was strongly in favor of heat as the active agent. It was uncertain whether the heat acts directly on the substance of the lens, or indirectly by disturbing its nutrition through deleterious action upon the tissue of the iris and the ciliary body, and, finally, that ultra-violet radiation may possibly play some part also by indirect action on the nutrition of the lens.

While it is entirely possible to avoid danger by means of protective glasses, it is very difficult to compel workmen to wear them.

GLASS-WORKERS' CATARACT IN PUDDLERS, TINPLATE MILLMEN AND CHAIN MAKERS. It is now conceded that the cataract observed so frequently in glass-blowers is caused by the infrared rays coming from the molten glass, assisted perhaps by the extreme heat to which the victim's eyes are exposed.

Cridland[2] states that among 1500 hands employed in one important iron plant, only 40 are engaged in the actual smelting or puddling process, and among these he has seen several cases of typical "glass-blowers' cataract."

Healy[3] has had the opportunity of examining the eyes of the men in the tinplate mills of Llanelly where 4 men worked at each mill—the heater, the doubler, the rollerman and the behinder or catcher.

[1] British Journal of Ophthalmology, October, 1921, p. 464.
[2] Ibid., May, 1921, p. 193.
[3] Ibid., p. 194.

The work is very heavy, and the heat great, so that the men perspire freely and drink a great deal of tea or beer. Since they enter the mill as behinders or catchers at about the age of eighteen, they are not exposed to the greatest heat or glare from the molten metal until they are promoted after a few years to furnace men, and usually the promotion to doubling comes in about five years, and again to rollerman after another five years. "All of the men in the mills are exposed to infrared rays from the red-hot tin plates."

On his first examination of the men in the X works, he found that 40 per cent of the men of thirty-five years of age and over had opacities of various types in the lens.

In his later examinations of the men in twelve works, he found, in 354 men of thirty-five and over, 144 with lenticular opacity, 5 of which were complicated, leaving 39 per cent.

In his total of 209 cases, he found the typical, wedge-shaped, striated opacity below with its apex upward, and growing into the posterior cortex in 105 cases; dense cortical opacity in 26 cases; while 20 cases show a combination of these two forms.

St. Clair Roberts[1] also reports 25 cases of cataract in men and women engaged in chain making.

It is a matter of common belief among the workmen that their sight should begin to fail between the ages of fifty and sixty.

Subnormal Accommodation the Result of Focal Infection. The general practitioner should make a habit of warning all of his patients who are recovering from wasting disease, confinement, or surgical operations from straining the accommodation by reading or other close work on the ground that while the patient is still weak, the muscle of accommodation is as unfitted for near work as the muscles of the body are for heavy manual labor.

Percy Sumner[2] reports 3 cases of patients with tonsillitis who were suffering from symptoms of eyestrain, and who were found to have a subnormal accommodation. One of these cases was persuaded to have his tonsils removed, and three weeks after the operation the near point of the twenty-four year old man had advanced from $8\frac{1}{2}$ inches, age thirty-eight, to $5\frac{1}{2}$ to 6 inches, and two weeks later to 4 to $4\frac{1}{2}$ inches.

Contrary to the experience of some, Sumner has not found that focal infections from the teeth or the nasal sinuses cause weakness of the accommodation, but he has seen it associated with diseased tonsils in other patients than these here reported.

Neuro-allergic Conjunctivitis. It will be remembered that Schnaudigel[3] believed that he had had striking results with tuberculin in the treatment of certain dry or chronic catarrhs with marked photophobia, and inability to do near work, which had seemed incurable by all other treatment. ("Copiopia Hysterica" of Foerster.)

He, therefore, considers that the sensory nerves of the eye are rendered allergic and hypersensitive by toxins.

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[1] British Journal of Ophthalmology, May, 1921, p. 210.
[2] American Journal of Ophthalmology, May, 1921, p. 357.
[3] Klin. Monatsbl. f. Augenh., January, 1920, **64**, 70.

He begins with 0.000001 dosage, increasing every four or five days until 0.00001 is reached. About 10 injections have sufficed in 30 cases out of 40 patients treated in the last ten years.

Asthenopia. In his editorial on asthenopia,[1] Jackson rather confirms Elliott's view when he refers to the "altered conditions of living that finally produce a form of asthenia that leads the body to react, by pain, to what was once a normal stimulus." "Much the same is true of the consumptive. The long saturation of his nervous system by the toxins of the tubercle bacillus, while stimulating it to a reaction needed to combat the invasion that threatens the body's destruction, has also come to limit by pain the demands made by even the slight mental and physical effort of reading."

Pressure Astigmatism from Meibomian Cysts. Astigmatism from pressure has been a long recognized entity. Ormand[2] has reported 3 beautiful examples of temporary, acquired astigmatism apparently caused from the pressure of large chronic chalazia, which were hard and protuberant. All 3 patients complained of a gradual failure of sight, which they did not associate with the presence of the tumors. The amount of temporary astigmatism varied with the size of the tumor, and 1 case seemed to have increased hypermetropia as well as astigmatism. The retinoscopic shadows were broken up and whorled as in conical cornea.

The Relationship of Race to the Prevalence of Lacrimal Disease. In order to explain the scarcity of disease of the lacrimal passages in the negro as compared with its prevalence among Caucasians, Santos-Fernandez[3] made comparative measurements of the tear passages in whites and full-blooded negroes, and came to the following conclusions:

1. The lacrimal canal is longer in the white race than in the negro.

2. Negroes have a wider lacrimal canal than whites.

3. The distance that separates the lower orifices from the two canals is greater in negroes than in whites, this being the cause of the lower orifice of the conduit in relation to the upper being almost always outward in the negro.

4. In negroes the direction of the lacrimo-nasal canal tends to follow a direct line. The double bend in the lateral and antero-posterior is less marked than in the whites.

5. The lower orifice in the negroes corresponds to the roof of the inferior canal of the nasal fossa, being much larger and more rounded than in the white. In the white race this opening is narrow, more oval, and corresponds to the outer wall of the canal in almost all cases.

The nasal canal then in the white race is longer and follows a more tortuous course and this fact explains the greater tendency to obliteration or narrowing of its lumen in affections of the lacrimal passages, while in the negro it is wide and follows a straight course.

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[1] American Journal of Ophthalmology, March, 1921, p. 218.
[2] British Journal of Ophthalmology, March, 1921, p. 117.
[3] American Journal of Ophthalmology, January, 1921, p. 32.

The Influence of Age Upon the Axis of Astigmatism. Stirling[1] holds that the belief that astigmatism "according to the rule" and against the rule tends to remain permanent is not founded on fact, but that the axis of astigmatism rotates with advancing years, and that this fact applies to myopic as well as hyperopic astigmatism. Of 544 eyes, which he classified according to decades of life, 416 were hyperopic, and 128 were myopic. With few exceptions, he used only those eyes which showed an astigmatism of 0.5 and upward, and the average of hyperopia taken was 0.37 D and of myopia 1.02 D.

Of 107 hyperopic eyes under fifty years, 17, or 15.9 per cent, were more nearly horizontal than vertical, while of 309 hyperopic eyes over fifty years of age, 196, or 63.4 per cent, were more nearly horizontal. Of the 79 myopic eyes under fifty years of age, 54, or 68.3 per cent, were more nearly horizontal than vertical, and of the 49 myopic eyes over fifty years of age, 18, or 36.7 per cent, were more nearly horizontal than vertical.

"It seems fair to conclude from the above series of figures that we must modify the so-called 'rule' for astigmatism, which appears to be true for young eyes, but the reverse for the elderly," all of which tends to confirm teachers in their warnings to students not to rely on the cross alone, but to remember that the axis of astigmatism may be found in any position other than either vertical or horizontal.

Focal Adjustment in the Aphakial Eye. Lewis[2] reported the case of a man aged fifty-one years, who had been operated upon for congenital cataract in 1872 and 1878, and whose distant vision was 5/200 O. U. without glasses, and about 20/20 with his cataract lenses. With his distance correction, he could read J. I. at 7 inches with both eyes and with the left eye he could read J. I. at 9 inches, and after a few minutes effort could carry the same print as far as 18 inches and continue reading. When the left eye was opened and binocular single vision was attempted, he was again able to bring the print back to 7 inches.

Lewis truly says that a man with normal eyes and aged fifty-one years, would have a remarkable amplitude of accommodation from 18 inches to 7 inches, and gives expression to the opinion that since the eye of the ox seems to have a vitreous of much greater consistency at its middle than in the periphery, and since nature is chary of duplicating her methods, it is probable that those cases of apparent accommodation in aphakic eyes are in reality genuine cases of accommodation through the medium of a "vitreous lens."

Jackson,[3] however, calls attention to the fact that one part of the vitreous may be more firm than another and still have the same index of refraction as do the solid cornea and the liquid aqueous.

Certainly the theories so far brought forward do not hold water in many cases, and although every ophthalmologist has seen such instances, their mechanism still remains unexplained.

Objective and Subjective Tremors as Functional Disorders Due to

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[1] Archives of Ophthalmology, January, 1921, p. 19.
[2] American Journal of Ophthalmology, April, 1921, p. 258.
[3] Idem, p. 298.

Eyestrain. Kahn[1] reports 647 cases of subjective and objective tremor of which number 126 men reported after their error of refraction had been corrected and 172 women. Of these, 109 men, or 85 per cent, and 154 women, or 90 per cent, reported improvement or cure. By objective tremors he means those which are absolutely visible and demonstrable to touch and are always accompanied by other symptoms. They are slow and moderate, fine or coarse, and usually volitional, being always functional and not organic. The hands and arms are most frequently involved, next the legs and occasionally other sets of muscles, as the chin, tongue, cheeks, spine muscles, etc.

Subjective tremors are simply the feeling of tremors, which the patient may experience in the chest, body, abdomen, arms, legs, etc., which are demonstrable to the investigator.

One's first thought, upon reading the report and considering the taking of the history and asking questions about what has until this time been considered a rather intangible symptom, is whether perhaps suggestion may not have played a part in eliciting it, but his great number of cases, and the signs demonstrable to him lead one to be on the lookout for this clinical entity connected with strain of the accommodation.

Glaucoma. THOMPSON'S THEORY OF THE PRODUCTION OF GLAUCOMA. Vaidya[2] attempts to explain the fact that an attack of acute glaucoma so frequently appears between midnight and early morning, *i. e.*, after a few hours of sound sleep, by reviewing Arthur Thompson's theory. The latter has called the triangular projection around the inner side of the sclera, posterior to the opening of Schlemm's canal, the "scleral spur." The elastic ligamentum pectinatum is attached to its anterior aspect or apex, and the fibers of the ciliary muscle to its posterior aspect or base. Accommodation pulls the scleral spur backward, pulling the walls of Schlemm's canal apart and also stretching the ligamentum pectinatum, thus causing a negative pressure in the canal and an inrush of aqueous into the canal. When the ciliary muscle ceases to act, the pectinate ligament, in returning to its normal condition, produces positive pressure in the canal, and the fluid is pumped onward into the anterior ciliary veins. Since accommodation ceases during sleep, under normal conditions the supposedly constant secreted aqueous probably escapes through the crypts of the iris, and posteriorly through the lymphatic channels of Cloquet's canal. In eyes predisposed to acute glaucoma, "the comparatively scanty filtration is not adequate until the morning hours when the patient wakes, and the pumping mechanism can come into play again." While this theory seems plausible, the question of what pathologic process causes the predisposition to glaucoma still remains unanswered.

THE OPERATIONS FOR GLAUCOMA. Tulieres and Pesme[3] discuss the various operations which have been devised since the first iridectomy of von Graefe, in the treatment of chronic glaucoma.

[1] American Journal of Ophthalmology, June, 1921, p. 438.
[2] British Journal of Ophthalmology, April, 1921, p. 172.
[3] Arch. d. Oph., April, 1921, p. 215.

In the last few years, because of the large number of unfavorable complications which have been reported, there appears to be a certain rebound from the fistulization methods, such as those of Holth, Lagrange and Elliot.

The authors have reached the conclusion that the ideal operation in chronic glaucoma is simple sclerectomy with peripheric iridectomy.

THE TREPHINE IN CHRONIC GLAUCOMA. Since the trephining of the sclero-corneal margin in glaucoma was introduced by Elliot, late infections of the eye in the wound region have been the *bête noir* of operators. It is therefore refreshing to note the frank change of opinion of so eminent a surgeon as T. Harrison Butler[1] who expressed adverse views six years ago[2] as to the safety of the trephine operation.

Having suffered the disappointment resulting from several cases of late infection, he abandoned trephining and again resorted to iridectomy in a series of cases of chronic and subacute glaucoma. A careful analysis of all of his cases of iridectomy showed but 43 per cent of permanent relief as against 64 per cent of successes from trephining compiled to the same date. He also found that while the Holth punch was more successful in reducing tension than the 1.5 mm. trephine, nearly all the cases of late infection had followed the punch operation. He then began to use the 2 mm. trephine, and has had most gratifying results. During 1918 and 1919, he has trephined 80 eyes in 70 subjects. Forty odd of these were for glaucoma simplex. Combining these with his former operations, he finds that in 100 cases of trephining he has had 77 per cent of successes and adding 3 more recent successes out of his 23 failures, he now has a percentage of 80 to date. He therefore believes that trephining performed early with a 2 mm. trephine is the operation of choice. He does not believe that miotics avail in those cases in which the pupil and anterior chamber are normal. The indication for the operation are continued high tension and narrowing of the field with a Bjerrum scotoma, and, when a late infection does occur, it is to be regarded as part of the toll taken by glaucoma, the good results still overshadowing those of any other operation.

FINAL OUTCOME OF GLAUCOMA OPERATIONS. Since the visit of Colonel Elliott to this country several years ago, much interest has been taken in the comparative estimate of recoveries from glaucoma after the various operations *viz.*, the old broad iridectomy, the excision of a small piece of sclera at the limbus (Lagrange), Elliott's trephine of the corneal limbus and its various modifications, such as the Bradley's punch. Much has been written about later infections through the filtering scar, and also the effect of the operation upon the disease itself, but little has appeared concerning the avoidance of continued injury to the optic nerves, which finally resulted in blindness after the glaucoma has been "cured." A case of my own recovered normal intraocular tension, but the vision gradually but surely diminished after a trephining in 1916.

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[1] Archives of Ophthalmology, January, 1921, No. 1, **50, 1.**
[2] Ibid., 1915, No. 6, **44,** 611.

Tresling[1] reëxamined 13 cases of corneal-scleral trephining some years after the operation, and found that the vision had steadily declined, and the fields had become more and more narrow. While he had anticipated this result in his iridectomy cases (Why? Ed.) he was greatly disappointed to find it also after trephining.

THE ACTION OF ADRENALIN ON THE GLAUCOMATOUS EYE. Knapp[2] has examined a series of 65 eyes with primary glaucoma after instilling a drop of adrenalin every few minutes for five times. The tension and measurement of the pupil were taken beforehand, and also a half hour after instillation. Cases with atrophic irides and posterior synechiæ were excluded.

Of the 65 cases, the pupil dilated from 1 to 5 mm. in 60, the intraocular pressure was unaffected in 40, diminished in 20, and increased in 3 cases. The adrenalin mydriasis can usually be promptly corrected by miotics.

In 15 cases where the other eye was normal, the normal eye showed in 12 a dilatation of the pupil after adrenalin, in 3 there was no change, the intra-ocular tension was unaffected in 12, in 3 the tension was reduced. "This suggests that a susceptibility to adrenalin may be present long before the usual clinical signs of glaucoma."

The Influence of Adrenalin on the Ocular Tension and on the General Retinal Blood Tension in Man. George Leplat[3] observed 22 cases ranging in age from sixteen to thirty-seven years, in which $\frac{1}{2}$ cc of the 1 to 1000 solution of adrenalin (Parke, Davis & Co.) was injected under the skin of the arm. The variations of the general arterial tension were measured by the method of Riva-Rocci for the systolic tension, and by the oscillometer of Pachon for the diastolic. Baillart's technic was applied in determining the tension of the central retinal vessels. The apparatus of Schiötz was used two to seven times in the forty minutes following the injection to determine the ocular tonometry.

In the majority of cases, the pulse was accelerated from 20 to 30 to the minute. The hypertension varied from 5 to 75 mm. Hg (humeral). The diastolic, measured on the radial, presented a curve less accentuated and the hypertension never exceeded 30 mm. of Hg. It was often less, sometimes nothing. Twice it even dropped below the initial figure.

In every case observed the systolic pressure of the central retinal artery has followed a curve parallel to that of the general systolic tension, but ordinarily with less amplitude. No augmentation of the ocular tension was observed in any of the 22 cases.

Injuries to the Eyes of Children. In the Glasgow Eye Infirmary, during 1917, 1918, and 1919, Buchanan[4] found that 61 eyes had been excised after injuries to children, and granting about 50 per cent of seriously injured eyes are excised, he figures the total loss at 120, or 40 per annum, a greater toll than that taken by ophthalmia neonatorum.

[1] Nederlandsh Tijdschrift v. Geneeskunde, May 21, 1921, p. 2802. Abstract, Journal of the American Medical Association, August 6, 1921, p. 502.
[2] Transactions of the American Ophthalmology Society, 1921, Archives of Ophthalmology, November, 1921, p. 556.
[3] Annal. d'Ocul., June, 1921, p. 414.
[4] British Journal of Ophthalmology, January, 1921, No. 1, **5**, 14.

The majority of these cases were manifestly preventable, as is shown by the following table:

Stones thrown	21
Explosion of cartridges and caps	5
Glass thrown	10
Iron wire	5
Tin cans	5
Fork (loosening bootlace)	2
Pen knives	4
Scissors	2
Kick of a horse	1
Door key	1
Button hook	1
Thorn	1
Airgun pellet	1
Steel spring	1
Pencil (in school)	1
Total	61

"They are only too frequently the results of a display of temper, or of carelessness in playing, or being permitted to play with dangerous articles."

The Frequence of Syphilis in the Etiology of Iritis. Clapp[1] refers to the work of Irons and Brown[2] who found only 23 per cent of syphilis in 100 cases of iritis, and also a report from the Wills' Eye Hospital by Jennings and Hill[3] who gave 61.4 per cent as due to syphilis. He himself has tabulated the last 87 cases of acute iritis, which came to his clinic, and added 13 other cases from his private practice; 43 of the clinic group gave a positive Wassermann, which cleared up under treatment *i. e.*, 49.4 per cent; 20, or 33.3 per cent, were diagnosticated clinically, and were relieved by specific treatment.

His conclusions were that syphilis is the etiologic factor in about 80 per cent of acute cases of iritis, two-thirds of the cases are male and 8 per cent of the cases show condylomata of the iris.

Syphilitic Iritis, Its Racial Influence and Its Association with Secondary Syphilis and with Neurosyphilis. Zimmermann[4] notes that both in early secondary syphilis and subsequently in the course of the disease, the negro is more liable to iritis than is the white man, since it occurs in more than 10 per cent of all cases of early secondary syphilis in the negro, and it is also most often associated with follicular syphilides.

It has been a mooted question with writers whether neurosyphilis is more liable to follow in those patients who have had iritis than those who have been free from syphilitic affections of the uveal tract. While Fuchs, Wernicke and Wintersteiner considered iritis an assurance against the eventual development of tabes and paresis, and Syndacker did not find any changes resulting from a previous uveitis in 61 tabetics and not once did he observe the eventual development of tabes or paresis in 79 cases of syphilitic iritis and 42 of choroiditis; yet Trousseau, in 40 cases of syphilitic iritis, observed 3 subsequently developed paresis,

[1] American Journal of Ophthalmology, March, 1921, p. 194.
[2] Journal of the American Medical Association, 1916.
[3] Ophthalmology, April, 1909.
[4] Journal of the American Medical Association, June 25, 1921, p. 1818.

12 tabes and 8 other forms of neurosyphilis; Mattauschek and Pilez found 10.96 per cent of paretics had at one time had iritis, Igersheimer found changes in the spinal fluid in 6 or 8 cases of acute iritis; and Wile and Marshall in 21 cases of secondary syphilis with iritis found 15 with definite spinal fluid abnormalities, while in about one-half of 508 cases of secondary syphilis the cerebrospinal fluids were abnormal.

In 3 white patients in Zimmermann's series of iritides with secondary syphilis, none showed spinal fluid abnormalities, and of 13 negroes, only 2 were abnormal. Of 16 white patients in whom iritis occurred alone or with tertiary manifestations, 2 were found with pathologic fluids, while only 1 in 15 negroes showed a pathologic fluid. Of the entire series of 47 patients with iritis, only 6, or 12.8 per cent, were neuropathologic.

High Degree of Myopia. Myopia of high degree is usually acquired and associated with disease of the choroid which increases with age, the so-called malignant type.

Kimberlin[1] reported a case of myopia in a child aged five and a half years whose vision in 1917 was 3/60 right eye, 2/60 left eye.

Examination revealed right eye—16 D, and left eye 18 D—which was corrected under full atropine cycloplegia; school was prohibited as well as all books except those with largest print. The vision is now 5/9 in each eye and the slight stretching at the disk has not increased.

Oliver[2] reported the case of a man aged thirty-five years, who had served two years in the Army in a labor battalion, one year of which time he was in France.

Retinoscopy revealed right eye—60 D and left eye—24 D, his vision being without glasses 1/60 in each eye. With correction his vision was 3/60 and 6/60.

The fundus was normal in each eye except for a small myopic crescent. He believes that the absence of fundus changes, and the fact that the eyes are not prominent shows that the condition is probably congenital, the orbit having increased in size with the growth of the eyeballs. No x-ray had been taken of the orbits.

Arteriosclerosis of the Arteria Centralis Retinæ. Scheerer[3] summarizes his findings in a case of double-sided closure of the central artery found post mortem in a man afflicted with leutic arteriosclerosis.

He states that arteriosclerosis of the central artery, apart from diffuse changes in the neighborhood of the lamina cribrosa, can occur in two characteristic forms, which can lead to complete stoppage of the circulation:

1. A concentric narrowing under the picture of "a new tube in an old" and a high grade fatty degeneration of the intimal thickening.

2. A humplike narrowing with tendency to calcification sometimes lying apparently free in a dilated lumen.

Finally, other causes (hemorrhages, inflammations, in isolated instances probably true emboli also) can lead to blocking of the circulation.

[1] American Journal of Ophthalmology, January, 1921, p. 43.
[2] British Journal of Ophthalmology, February, 1921, p. 68.
[3] Klin. Monatsblätt. für Augenheilk., 1921, p. 599.

Ocular Symptoms in Hypophyseal Disease which is Coincident with Acquired Syphilis. de Schweinitz[1] calls attention to the fact that acquired syphilis of the hypophysis does not cause any characteristic symptoms which differ from those of disease of the gland from other causes, although it may be that a careful statistical record would show more ocular palsies among such patients who have syphilis than among the others.

In the cases which he reported, the patients exhibited a marked tolerance to mercury, even though they were not apparently otherwise syphilitic.

Admitting that glandular therapy should be used in those cases with hypopituitarism, and perhaps a polyglandular therapy, he believes also in the good effect of mercury, which, if it is not in a given case specific, yet adds to the therapeutic effect of other treatment. It has long been known that mercury stimulates the action of certain glands, and it is possible that this action may extend to all glands.

Therefore, if a patient with acquired syphilis exhibits symptoms of hypophyseal disease, active specific treatment may show brilliant results and should be instituted at once. If, however, symptoms are unaltered or grow worse under adequate specific treatment, then one can feel that the disease of the gland is not luetic and, therefore, other measures must be undertaken.

He emphasises the importance of thorough ophthalmoscopic examinations of all patients with hypophyseal symptoms and especially of the periphery of the fundus after dilatation of the pupil in order not to overlook luetic lesions. "This is particularly true of congenital lues, where other stigmata of this disease may not be conspicuous."

Timme[2] explains de Schweinitz[2] observation that the administration of thyroid enhances the effect of specific therapy by saying that luetics with central nervous system infection show signs of dyspituitarism. Thyroid activity being dependent on the iodine content of the body is lowered by the administration of mercury, arsenic and lead, which combine with the iodine. "We should, therefore, administer iodine and thyroid when we prescribe the heavy metals."

Stieren[3] reported the case of an adult male with Timme's pluriglandular syndrome and having a hemianopsia of the right eye and loss of central vision; also later an encroachment of the left field. X-ray revealed sella enlargement. There was general improvement in the field, and finally restoration of central vision after treatment by whole pituitary substance.

The Control of Pituitary Lesions as Affecting Vision by the Combined Surgical-X-ray-Radium Treatment. According to Frazier,[4] 90 per cent of cases seek relief because of failing vision and 8 per cent because of headache with or without failing vision. Exceptionally, there may also be other disturbances of pituitary function, such as adiposity, sexual apathy, amenorrhea; but the vast majority present pressure symptoms, which

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[1] Archives of Ophthalmology, May, 1921, p. 203.
[2] Ibid., May, 1921, p. 271.
[3] Transactions of American Ophthalmology Society, 1921.
[4] Archives of Ophthalmology, May, 1921, p. 217.

are the chief indications for surgical intervention. Frazier also notes the well-known fact that it is surprising how late the disease is diagnosticated. His records show that 24 per cent were totally blind in one eye when he was first consulted, and 21 per cent were practically blind in one eye or a total of 45 per cent, and in 6.5 per cent there was total blindness.

Hemianopsia was the most constant ocular finding, and there was a choked disk in only 5 per cent.

Pressure upon the commissure may be relieved by one of several procedures:

1. Sella decompression.
2. Sella decompression with excavation of the lesion.
3. Sella decompression followed by radium and x-ray therapy.
4. Suprasella subtotal extirpation.

If the lesion has decompressed itself by erosion of the floor of the sella turcica, the removal of the floor of the sinus may be of advantage because the radium will be more effective when its action is not obstructed by a layer of intervening bone as it is applied through the nasopharynx.

Of course, when the sinus has already been encroached upon by the lesion, there is no object in performing the sella decompression.

There is no reliable means of determining whether the diaphragm has been ruptured and the lesion has already extended intracranially. Atrophy of the clinoid processes implies such a condition, but in the earlier stages of the lesion the posterior clinoid processes may be still intact.

When decompression downward has given temporary relief of visual disturbance, and recurrences later follow, one may infer that there has then occurred an extension upward.

"A SIMPLE SELLA DECOMPRESSION IS INDICATED (*a*) when there is no striking evidence of intracranial extension and (*b*) when there has not been a spontaneous decompression. THE SUPRASELLAR APPROACH IS TO BE CHOSEN (*a*) when spontaneous decompression has occurred, and (*b*) when there is positive evidence of an intracranial extension" subject of course to certain practical considerations, one of which is the possible use of radium and the x-ray. Therefore, if an operation is indicated, Frazier does a simple subsella decompression with incision of the capsule without attempting extirpation of the growth. "Should there be a recurrence of visual disturbance, x-ray and radium are employed by an experienced roentgenologist. If, despite these, the condition is not under control, to prevent blindness the lesion is exposed by a transfrontal craniotomy, and removed in whole or in part."

The Retinitis of Diabetes Mellitus. Wagener and Wilder[1] consider that a retinitis characteristic of diabetes as compared with that of nephritis must be regarded as unproved in spite of those writers who claim to see ophthalmoscopic differences.

In 1890, Hirschberg divided the retinal lesions of diabetes into three groups:

1. A central punctate retinitis characterized by small white spots sometimes accompanied by hemorrhages.

[1] Journal of the American Medical Association, February 19, 1921, No. 8, **76**, 515.

2. A retinitis hæmorrhagica with degenerative changes.

3. Rarer forms of inflammation and degeneration not yet classified. He believed that central punctate retinitis is due to diabetes alone, but that perhaps the accompanying edema and exudates may be suggestive of nephritis, and placed these under a fourth group, also that the hemorrhagic form is usually associated with arteriosclerosis.

The authors' series of 44 cases were taken from the study of 300 cases with diabetes. Eighty of these were of acute onset, progressively increasing severity (the so-called diabetes gravis), and none of these showed retinal changes. Retinitis appeared exclusively in those patients with mild, easily-controlled glycosuria in whom evidence of vascular disease was always present. However, they were impressed with the fact that the retinal lesions were in some respects different from those in non-diabetic vascular disease. All of Hirschberg's types occur and any one of them except the third should suggest diabetes even in the temporary absence of sugar. The retinitis of diabetes is therefore the retinitis of cardiovascular-renal disease modified by appearance and stage of occurrence possibly by metabolic disturbances associated with the diabetes. In the most common type of diabetic hemorrhagic retinitis, the hemorrhages are small or of the large, round, nuclear-layer variety like those of pernicious anemia and leukemia. Altered composition of the blood has been suggested as a cause, and moderate vascular and renal involvement is a constant factor. The superficial flame-shaped hemorrhages seen in diabetes seem to be dependent on advanced vascular and renal changes.

Diabetes in Relation to Diseases of the Eyes. In Doyne's[1] report of the discussion of this subject by the Ophthalmic Society of the United Kingdom in 1920, Garrod stated that while diabetic retinitis is somewhat similar to albuminuric retinitis in appearance, yet the former is seen only in the elderly, while albuminuric retinitis is met with at any age. All observations tend to show that retinitis in diabetes is not necessarily to be attributed to sugar in the blood nor to acetone bodies, but rather to cardiovascular changes and that diabetic retinitis is associated with increase of blood-pressure. In his own cases of diabetic retinitis, he found evidence of renal disease.

The view that the withdrawal of water from the lens, by reason of the presence of sugar in the aqueous, is the cause of cataract is no longer tenable, since the amount present is insufficient, and sugar has been found in the lens itself. The cataract must be the direct outcome of a disordered metabolism.

Foster Moore said that the retinal lesions may be differentiated from the renal and arteriosclerotic forms by the following characteristics:

(a) "The patches of exudate tend to have sharp-cut edges, are often solid and soapy looking, and frequently distributed unevenly or in an irregular ring wide of the macula.

(b) The star-shaped figure is seldom seen.

(c) The soft edged cotton-wool patches, common in renal cases, do not develop.

[1] Archives of Ophthalmology, July, 1921, p. 278.

(*d*) Retinal hemorrhages tend to be in the deeper layers, and so are roughly circular in outline, and are usually well wide of the central region.

(*e*) Circular retinal pigment spots, seen in the late stages of renal retinitis, are not seen."

While the histological examination of the eyes of diabetics almost always shows swelling and proliferation of the pigment epithelium of the iris, the clinical evidences of iritis are seldom seen, yet do sometimes occur.

LIPÆMIA RETINALIS HARDLY EVER OCCURS EXCEPT IN DIABETES and requires about 5 per cent of fat in the blood for its appearance.

The Genesis of Albuminuric Retinitis. Schieck,[1] in an article on the Genesis of Albuminuric Retinitis, gives a brief review of the three theories now current to explain this ocular condition. The first two are the well-known toxic, due to poisons circulating in the blood as the result of defective elimination from the kidneys; and the vascular, where under the influence of the kidney disease the general circulatory system shows changes, which in the eye cause the pathological condition under discussion.

The third explanation was first introduced by Volhard in 1916. This author states that the albuminuric neuro-retinitis might be the result of an ischemia due to a contraction of the arteries. This ischemia must induce an insufficiency in the kidneys if it remains long enough. Schieck thinks this latter theory the correct one, at least this condition of ischemia could be established in all the cases he observed with Volhard.

Lipemia Retinalis. Lipemia retinalis is a sufficiently rare condition to make every reported case of interest. An excess of fat in the blood renders the veins and arteries alike, and of apparently equal size.

Cohen[2] stated that there were only 8 cases of this condition reported in the literature. It is a condition of such an increase of fatty bodies in the blood as to be discernible in the color of the vessels of the retina, and is usually seen in young male diabetics.

Cohen's case was a fourteen year old boy who in October complained of marked weakness, frequent urination, great thirst, and pain in the right leg. The diabetes had been first discovered in April. His condition had steadily grown worse in spite of fifteen weeks of hospital care.

The day after admission the ophthalmoscope was used while the patient was in coma. Both eyes were very soft (T–) both fundi were of the tesselated type. "This lack of pigment has frequently been referred to in diabetic cases, and should be noted." There were two small recent hemorrhages in the left eye. The well defined disks were grayish especially on the temporal side. The retinal arteries and veins were similar in all respects with an apparently slightly dilated lumen. The size and milky color of the veins and arteries were such that they could not be distinguished apart.

The blood-sugar thirty-six hours before death was 282 mg. per 1000 cc. The CO_2 combining power of the blood was 9 cc per 100 cc of plasma,

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[1] Klin. Monatsblätte f. Augenheilk., January, 1921, p. 39.
[2] Archives of Ophthalmology, May, 1921, p. 246.

about $\frac{1}{6}$ of normal, the lowest on record. The total fat-content was 8.95 per cent, over 10 times the normal: Cholesterol, 1.12 per cent, about 6 times the normal: Urea nitrogen 9.3: total chlorides 300 mg., about $\frac{2}{3}$ normal. Blood count 3,150,000 reds, hemoglobin 30 per cent, 15,600 white 76 per cent of which were polymorphonuclears, specific gravity of urine 1023 to 1028, marked increase of sugar, acetone and diacetic acid present. Death in forty-eight hours.

Hardy[1] reported the second case on record of recovery from this rare condition in a man, aged twenty-nine years, who was admitted to the Barnes Hospital on account of an eruption over the arms and legs, with rapid loss of weight and marked weakness, with increasing thirst, and nocturia for six months.

Urine—specific gravity 1028—acetone and diacetic acid strongly positive—six hours output 1560 cc.

Sugar—43.3 gm.—albumin faint trace, no casts.

Diagnosis—1. Diabetes mellitus.

    2. Xanthoma.

    3. Furunculosis.

    4. Syphilis, Wassermann four plus.

    5. Lipemia.

    6. Acidosis.

Blood, reds 4,400,000; whites, 8250 hemoglobin, 70 per cent to 80 per cent; differential, normal except for increase in lymphocytes to 35 per cent; P. S. P. 63 per cent in two hours. Blood sugar, 0.278 mgm. per 100 cc. Plasma CO_2 volumes per cent 343.

Serum showed marked lipemia, being of a creamy color. Cholesterol 780 mgm. per 100 cc, while control was 200 mgm. Fat estimation 9.5 per cent.

The patient was placed on a diet of 60 gm. of carbohydrates and thrice cooked food for six days. He received 160 grains of sodium bicarbonate in five hours. Blood plasma CO_2 volumes per cent 46. "Vessels appear as if filled with an emulsion." No retinitis or hemorrhages. Media clear. In six days the blood fat was 2.9 per cent. Under increasing proteid and carbohydrate diet the blood sugar diminished and in sixteen days the fundus examination showed a normal appearance. Discharge in one month after ulcerated tooth had been extracted, two furuncles opened, and one dose of arsphenamine given. Further treatment in the skin clinic.

"The color of the retinal vessels as described by Heyl, and others was that of a light salmon. In my case the color was more of grayish-white likened by me at the time of observation to the color of chocolate malted milk.

"Possibly the amount of retinal pigment present has a bearing on this point," Heyl's case was examined by gas light, Hardy's with an electric ophthalmoscope. The impression gained by looking at the retinal vessels was that of "flat ribbons twice the width of normal veins, filled with chocolate malted milk," and "absolutely devoid of the light streak."

[1] Transactions of the American Ophthalmology Society, 1920.

Heyl's explanation of the width of the vessels was based upon the supposition that in health the visible part of the blood comprises the axial stream of corpuscles while the peripheral part is invisible plasma. In lipemia the plasma becomes visible, and the vessel appears double its usual size. Hardy also states that according to R. Foster Moore the disappearance of the light streak is due to the ground glass effect of the opaque plasma, the cylindrical contour is lost, and the vessels appear flat.

Neuroretinitis Following Salvarsan Injection. The patient of Oden and White[1] was aged twenty-four years, and had normal vision when he was discharged from the army. In July, 1920, he contracted syphilis, and immediately consulted his family physician, who gave him salvarsan once a week for five treatments. The morning following the fifth injection, he noticed a blurred sensation in his right eye. The disk was swollen 4D, with cloudiness of the surrounding retina; the arteries were small and the veins tortuous. V-20/200 with central scotoma for green and red. The vision of the left eye was 20/20, fundus normal, and the paranasal sinuses were negative. The Wassermann was also negative.

Since the neuroretinal disturbance appeared less than four weeks after exposure and during the first week of the initial lesion, the authors believe that the cause lay in the idiosyncrasy to salvarsan, in spite of the denial of most authorities of the neurotoxic effects of that drug, but I would expect some other cause to appear from their report in December of the same year (viz., six months after the toxic substance had been introduced) that the condition of the affected eye remained the same. I have seen one case of thrombosis of the central retinal vein following the use of salvarsan, but I was not sure that the cause could be attributed to the drug.

Proliferating Chorioretinitis Following Injury. Lagrange during the war described a form of proliferating retinitis following injury which differs from the ordinary form in that it follows a hemorrhage and rupture of the deep membranes and presents a fibrinous plaque of more regular thickness, and more localized, than the multiple webs which extend over the greater part of the fundus in ordinary proliferating retinitis. It is also everywhere opaque instead of partially translucent, and has a simple relation of contact with the vitreous without the free extensions of the other form. It is located at the macula or in the vicinity of the papilla, and is usually accompanied by some pigmentation, and, finally, it is not accompanied by a detachment of the retina, but rather fastens it more firmly to the choroid.

Danis,[2] of Brussels, observed a man, aged twenty-five years, who was struck in the eye by a stone when he was seven years of age. The upper lid was divided, and vision immediately lost.

Danis found in front of the optic papilla "a gray, white mass, opaque, mammillated and cloudy, somewhat club-shaped, its rounded extremity extending up and outward." It protruded decidedly forward and sent two thread-like prolongations along the nasal inferior vein and artery.

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[1] American Journal of Ophthalmology, May, 1921, p. 365.
[2] Ibid., March, 1921, p. 153.

The posterior pole of the eye was slightly excavated behind it, and all around the papilla there was a circle of chorioditis with pigmentation. There was a pearl white spot with some pigment to the nasal side. The central vessels left the excavation of the posterior pole and ascended beside the white mass before spreading out over the retina. Lagrange believes that these lesions can be caused by a violent concussion of the bones of the face, which causes a concussion of the entire adipose system of the orbit. This causes rupture in the inner membrane of the eye, which latter are located in its most delicate part, *viz.*, the macula and the region of the optic nerve. This is twisted and twitched because it is firmly held by the attachment of the nerve to the apex of the orbit. Hence the ruptures and hemorrhages appear at the posterior pole of the eye.

Ocular Conditions Associated with Arthritis Deformans. After a cursory review of the literature concerning the ocular diseases which have been associated by ophthalmic writers with rheumatism and gout, Frieden-wald[1] states that nowhere had he found any definite mention of the connection between certain eye diseases and arthritis, which is now considered by most authorities a chronic joint affection caused by infection. The 4 cases are very significant, and give one cause for thought, although he admits that the problem is not solved. There was a scleritis in one woman, aged forty-one years, who had suffered from arthritis since she was fifteen years of age, almost all of her joints being affected. Her teeth were bad, and the tonsils and throat normal. There were marginal ulcers of the cornea in the other 3 cases, one associated with a chronic conjunctivitis.

Tuberculosis of the Eye and Allergy of Infants. T. Schieck[2] believes that he has demonstrated "The Dependency of the Course of the Tubercular Process in the Eye upon the State of the Allergy of the Body in General."

The therapeutic indication from his findings, he states, consists in protecting the organism against the return of a loss of allergy through a consistently applied course of tuberculin treatment, and thus to achieve the healing through immunity.

Neuroretinitis Eclamptica. E. Lindgren[3] states that among 10,200 births in ten years in his maternity hospital there were 74 patients with subjective visual disturbances, of which 12 had pathologic opthalmoscopic findings. The affection can appear in different forms (1) as a disease of the papilla, (2) as isolated focal disease of the retina in the form of white or yellowish-white plaques lying on the vessels in the innermost layers of the retina; (3) as a combination of 1 and 2 in the form of a neuroretinitis and (4) the papillitis can be accompanied by a detachment of the retina, which disappears without leaving any trace.

The Ocular Manifestations of Carbon Monoxide Poisoning. While acute and chronic poisoning from carbon monoxide have been described by a number of authors in general medicine, there has not been published any

[1] American Journal of Ophthalmology, June, 1921, p. 431.
[2] Archiv. für Ophthalmol Festhschr., Bd. **105**, p. 257.
[3] Ibid., Festschr., Bd. **105**, p. 286.

complete record of the ocular signs and symptoms in the ophthalmologic journals of recent years. The chronic form is that which most concerns the ophthalmologist.

Wilmer[1] recounted the details of such a case before the ophthalmic section of the College of Physicians of Philadelphia and stated that fortunately the newspapers keep the public informed of the dangers to life "of this gas in closed garages, from the instantaneous gas heaters (frequently in the bathroom) and from the common stove." It is well known that repeated inhalations of minute quantities are more dangerous to future health than one severe intoxication.

In chronic cases there may be "headaches, vertigo, tinnitus aurium, flashes of light before the eyes, weakness or absence of tendon and pupillary reflexes, nausea, pain in the epigastric region, palpitation, languor, muscular weakness and lack of coördination, convulsive movements, mental disturbances, hallucinations of sight and hearing."

The ocular sequelæ which have been observed are paralysis of ocular muscles, homonymous hemianopsia, paralysis of the third, retinal hemorrhages with congestion of retinal veins, "partial or complete blindness of varying duration, with or without ophthalmoscopic changes, xanthopsia, nystagmus, and paralysis of the eye muscles, and there have been repeated instances of complete ophthalmoplegia with marked protrusion of the eyeballs" (Edsall), and Wilmer also referred to de Schweinitz's quotation of Schnitz "Contraction of the visual fields partial color blindness, venous hyperemia in the retina and contracted arteries." Scotomata may also be present. The story by the mother of Wilmer's patient of the hallucinations of the whole family including servants make one of the most graphic stories of a haunted house ever written, the remarkable point being the striking similarity of the hallicunations of sight and hearing which the several victims experienced.

The history of the child first seen by Wilmer in 1907, when it was eight years of age, was that in October 1912 his parents moved into a house built in 1870, which was heated by a defective furnace. While all the family suffered from chronic carbon monoxide poisoning, this child alone seemed to have been affected, after removal from the several months' exposure to the gas, not only with gastric disturbance and anemia, but also by difficulty in reading. He miscalled letters although a clever boy. Two years before this his visual fields had been found contracted by Dr. Proctor. Wilmer found the eyes normal externally, pupillary reaction normal and motility and muscle balance good. Central vision was 20/20 in each eye. Fields much contracted. Fundi normal except that the disks were a trifle hyperemic. Color vision was normal.

In 1920, the patient was examined and brought the report that his vision was better. He now reads a great deal. The visual fields were much enlarged, but there was a marked paracentral scotoma in each eye. The blind spots were also enlarged.

When first seen by Wilmer, the patient seemed to be suffering from an interstitial inflammation of both optic nerves.

He concludes "that after a prolonged attack upon the tissues carbon monoxide exerts a deleterious influence, which is apart from its purely

[1] American Journal of Ophthalmology, February, 1920, p. 74.

oxygen-depletion effect, though the latter does sensitize the delicate structure of the central nervous system."

Ocular Manifestations of Onchocercosis. Onchocercosis is a new nosological entity characterized by a distinctly limited subcutaneous tumor, which contains a filaria of the onchocerca type, and whose principal symptomatology is shown in ocular disturbances. It is known as "Coast Erysipelas" and is endemic in Guatemala along the coast of the Pacific in an extensive strip of land having an altitude of 2000 to 400 feet.

The new parasite differs from the onchocerca volvulus of Leuckart in many respects. Its carrier has not been discovered.

Pacheco-Luna[1] gives Robles the credit of discovering the nature of the disease, the manifestations of which are principally seen in the form of eruptions on the skin of the face and scalp. In three days the face is swollen and the skin tight and puffed by a hard infiltration, which cannot be pitted by pressure as in edema, and which involves the eyelids, lips and ears, so that they are double their usual thickness. No change in the color of the skin, nor local differences in temperature can be observed as in erysipelas. The acute eruption is followed by a chronic form with mild manifestations.

The subjective sensations are photophobia, a drawing of the skin as if it would burst open and local irritation and itching.

The ocular manifestations include:

1. Horizontal, marginal, and inferior keratitis puncta superficialis.
2. Iritis fibrinosa with or without disturbance of the pupil.
3. Amblyopia without other appreciable symptoms; all types apparently characteristic of a type or a stage of the disease and age of the patient.

Improvement of vision can only be accomplished by operation on all tumors which can be found, and when sight is not improved the inference is that there exists somewhere in the patient's body an undiscoverable tumor.

Results with Tuberculin Treatment in Ocular Tuberculosis. S. Weigelin,[2] in an important article reviewed briefly, states that in respect to the literature before the year 1919 Hertel came to the conclusion that the value of treatment with tuberculin could not yet be clearly and definitely stated in spite of the many publications. V. Hippel among cases in his own material reported the greatest number of cases 75.7 per cent with tuberculin; 17.3 per cent improved only 7 per cent without result. In these statistics however, he took no account of the relapses, which in observations extending for three years occurred in 13 per cent.

The author, from his observations as assistant in the Tubingen University Eye Clinic where there was an especially large amount of ocular tuberculosis, and in his present work has gained the impression in much treatment with tuberculin that in the majority of cases an improvement could be obtained with the use of tuberculin, but that the occurrence of a relapse could not for the most part be prevented.

Professor v. Schlieck, his chief at Tubingen, stated, in one of his publications in 1906, that he could recommend tuberculin treatment on

[1] American Journal of Ophthalmology, March, 1921, p. 175.
[2] Klin. Monatsblätt. f. Augenheilk., 1921, p. 611.

the strength of his experiences. He believes that undoubted results occur in many cases, and that with cautious handling he saw no harm done in any case.

Abelsdorff, in 1920, reported similar findings, although he says it is to be added that in many cases the tuberculin is unable to influence the progress of the disease.

Hess, in 1920, stated, on the other hand, that from his observations the tuberculin treatment had no influence upon the course of the disease.

Igersheimer reported, in 1920, on the results from treatment with tuberculin at the Göettingen Clinic. He found that there was a good effect in the more benign forms of serous and sero-plastic iritis, but that in the severe cases of chronic irido-cyclitis and uveitis the tuberculin had no apparent effect.

Kollner said from the reports in the literature taken collectively, the question as to whether the phlyctenular process is affected by tuberculin is to be certainly answered in the affirmative, both in regard to healing of the eruptions and also in regard to the frequency of relapse. In this particular, the author (Weigelin) is of the opinion from his experience that in phlyctenular disease the value of tuberculin is more difficult to decide than in tubercular diseases of the uvea.

The author, coming to his own work at the Charlotte Hospital in Stuttgart extending over a period of eleven years, reports the findings with tuberculin in 77 cases of ocular tuberculosis who had been observed for periods from three to fifteen years. In 22 of these cases there could not be found from the history or by general physical examination any hint or trace of tubercular disease in any other organ of the body. Fifty were female and 27 males; 60 cases occurred between ten and forty years of age, the greatest number in any decade being from ten to twenty years. The author divides his cases into 3 classes and gives his results with tuberculin in the following table.

	No. of cases.	Relapses.	Cures.	Improvement.	Unfavor. course.
1. Iritis serosa and seroplastic choroiditis disseminata without typical tubercular signs . .	43	18	15	16	12
2. Typical iritis with tubercles; also choroidal tubercles . . .	22	15	11	6	5
3. Kerato-iritis tuberculosa and kerato-conjunctivitis eczematosa	12	7	6	4	2

The Ocular Menace of Wood-alcohol Poisoning. Ziegler[1] concluded that "wood-alcohol is the most deadly poison used in daily commerce," one teaspoonful having been known to cause blindness, and one ounce, death. Its port of entry is through the mouth, nose, or skin. It should be identified by Robinson's test.

It has a selective affinity for the delicate nerve tissues of the eye, and its biochemistry is "modified by oxidation, first to formaldehyde, and

[1] British Journal of Ophthalmology, September and October, 1921, p. 411.

then to formic acid, both of which are corrosive poisons, the latter being an end-product, which is excreted by the kidneys and which promptly reduces Fehling's solution, thus sometimes causing a false diagnosis of diabetes."

Acidosis in the first stages and alkalosis in the later stages are revealed by van Slyke's test.

"Sudden blindness with vomiting, and abdominal pain should always arouse suspicion of methylic poisoning, especially if diplopia or ptosis is associated." "Papillitis, sector-like atrophy, and sudden sclerosis of the nerve head are equally typical fundus lesions."

"Symptoms of pituitary injury are most suggestive in pointing to this as the primary and fundamental lesion." "Contracted fields and central or paracentral scotomata are usually present."

Early neutralization by alkalies, elimination by lavage, emetics, diaphoretics with stimulation of the optic nerve by negative galvanism applied directly to the eye are recommended by Ziegler and "Thyroid extract and pituitrin may be indicated."

Ziegler's suggestions are worth while in regard to regulation of the sale of wood alcohol with proper warnings and safeguards instructing the public against its use. He recommends an equalizing tax between denatured alcohol and methyl alcohol, which would remove the temptation to adulteration because of cheapness.

"All wines, whiskies, toilet articles and patent medicines imported from foreign countries should be tested for wood alcohol before passing through custom inspection. The name 'METHANOL' specially designates this product and yet avoids the tempting suggestiveness of the word 'ALCOHOL.'

Ocular Reactions in Anaphylaxis. Kodama[1] has found that horse serum applied to the eye of normal and sensitized guinea-pigs first causes "dilatation of the lids and pupil succeeded by contraction," the response being more prompt in the sensitized animals and also more vigorous. Anaphylactic intoxication with horse serum may also be associated with circulatory disturbances, edema, and congestion of the lid, conjunctiva, iris and fundus, with epibulbar and retinal hemorrhages.

Direct application of horse serum may cause vascular dilatation in the normal animal, and sometimes hemorrhage, but this is more apt to occur in the sensitized animal, and also independently of asphyxia, hence due to direct action on the vessels. In addition to the usual postmortem appearances of anaphylactic shock (dilatation of the lungs congestion and hemorrhagic extravasation) there is a rapid and strong contraction of the pupil after anaphylactic death.

ANAPHYLAXIS AS A MODE OF TREATMENT OF INTRAOCULAR HEMORRHAGE OF ADOLESCENTS. Dufour's view that anaphylaxis has an anti-hemorrhagic action seems to find some support from Aubineau's[2] report of 15 cases of intraocular hemorrhage in adolescents which are characterized by recurrences, invasion of the vitreous and retinitis proliferans.

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[1] Journal of Infectious Diseases, January, 1921, p. 48, Abstract, Journal of the American Medical Association, February, 1921, p. 406.
[2] Bulletins et Mémoires de la Société française d'Ophtalmologie, 1920, Abstract, British Journal of Ophthalmology, September, 1921, p. 426.

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